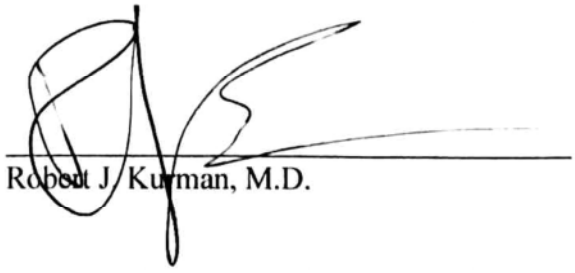
Exhibit A

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION ***THIS DOCUMENT RELATES TO ALL CASES***	**MDL NO. 16-2738 (FLW) (LHG)**

EXPERT REPORT OF ROBERT J. KURMAN, MD, FOR GENERAL CAUSATION *DAUBERT* HEARING

Date: February 25, 2019



Robert J. Kurman, M.D.

PROFESSIONAL BACKGROUND

I am currently the Emeritus Richard TeLinde Distinguished Professor of Gynecologic Pathology at the Johns Hopkins University School of Medicine, with appointments in the Departments of Pathology, Gynecology and Obstetrics and Oncology. Prior to my retirement in June 2017, I held senior academic positions at the University of Southern California, Georgetown University School of Medicine, and the Johns Hopkins University School of Medicine, Baltimore, Maryland, where I was since January 1989.

I graduated from the Upstate Medical Center at Syracuse in 1968 and did my pathology and obstetrics/gynecology residencies in Boston, at the Peter Bent Brigham, Boston Hospital for Women (now the Brigham and Women's Hospital) and Massachusetts General Hospital, as well as the University of Southern California in Los Angeles. I later served as the Assistant Chief of Breast and Gynecologic Pathology at the Armed Forces Institute of Pathology, Washington DC.

I edited the 3rd, 4th and 5th editions and co-edited the 6th and 7th editions (Senior Editor) of Blaustein's Pathology of the Female Genital Tract and served as co-editor (Senior Editor) of the World Health Organization Classification of Tumours of the Female Reproductive Organs (4th Ed.). As the co-author of 287 original papers, 154 review articles and book chapters and 15 books, I have made seminal contributions to our understanding of the pathology of tumors of the female reproductive organs, including gestational trophoblastic neoplasia, cervical, vulvar, vaginal, endometrial and ovarian cancer. These have led to several awards, including the Fred W. Stewart Award of the Memorial Sloan Kettering Cancer Center (2009) and the Maude Abbott Lectureship of the United States and Canadian Academy of Pathology (2012). I have served as President of the International Society of Gynecological Pathologists (2006-2008) and am an Honorary Fellow in the Royal College of Pathologists (2013) and the Austrian Society of Pathologists (2015).

I have served on the editorial boards of numerous journals and was Chairman of the Second Bethesda System Conference of the National Cancer Institute (NCI), Bethesda, 1991. I was Principal Investigator on several major NCI and Department of Defense funded research projects on cervical, vulvar and ovarian cancer. I have been invited as a visiting professor and given invited lectures, including multiple keynote lectures, numerous times in the United States and throughout the world. I have demonstrated my commitment to postgraduate training by the training of over 50 fellows. Additional information about my background, qualifications and publications can be ascertained from my CV, which is attached as Exhibit A.

The opinions expressed in this report are based on my education, training and experience, as well as my clinical/scientific research, knowledge of the literature, and the information available to me at this time. They are expressed to a reasonable degree of medical and scientific probability. I reserve the right to amend or supplement my opinions, should any additional information be made available to me or if I learn of additional scientific literature that is relevant to this case. I also reserve the right to amend or supplement these opinions in response to claims made by plaintiffs' experts. The footnotes and appended materials list contain many of the sources that I have considered in formulating my opinions, but given the size and scope of literature with which I am familiar, it is impossible to definitively list all sources considered.

I am being compensated at a rate of $500 per hour for consulting on this matter.

I. PATHOLOGY OF EPITHELIAL OVARIAN CANCER

Much, but not all, of the data referred to in this section are based on studies performed by me, Dr. Ie-Ming Shih and our colleagues in the Division of Gynecologic Pathology at the Johns Hopkins Hospital. In this report, I will describe the morphologic, immunohistochemical and molecular genetic features that underscore the heterogeneity of epithelial ovarian cancer and demonstrate that this cancer is a family of related but distinct tumors with different genetic features, clinicopathologic characteristics and behaviors. A more detailed description of the molecular genetic features of the various subtypes of ovarian cancer is provided in Appendix 1. I have also included a glossary of selected pathology terms that appear in this report in Appendix 2.

Ovarian tumors can be divided into five main categories: epithelial ovarian cancer ("EOC"), germ cell tumors, gonadal stromal tumors, miscellaneous tumors and metastatic neoplasms.[1] EOCs are the most common ovarian malignancies and are the types of ovarian tumors relevant to this case. EOCs include several different histologic types, which can be grouped into two broad categories, type I and type II tumors.[2,3] This dualistic model of ovarian carcinogenesis was proposed by me and my colleague, Dr. Ie-Ming Shih, approximately 10 years ago and has been revisited and revised to incorporate the many additional molecular genetic and pathologic studies that have been conducted since then.[4] The dualistic model is widely accepted in the field, as evidenced by the fact that our paper was the most frequently cited paper in the American Journal of Pathology in the last year.

Type I tumors are comprised of three groups: (1) endometriosis-related tumors, which include endometrioid, clear cell and seromucinous carcinomas; (2) low-grade serous carcinomas; and (3) mucinous carcinomas and malignant Brenner tumors.[5] Type I tumors are generally slow growing, present in early stage (stage I, confined to the ovaries) and are characterized by mutations that target specific cell signaling pathways, including *KRAS, BRAF, ERBB2, CTNNB1, PTEN PIK3CA, ARID1A* and *PPP2R1A*; only rarely are mutations of *BRCA1, BRCA2* or *TP53* involved (exception is mucinous carcinoma, in which *TP53* mutations can occur relatively frequently).[6,7,8] Type I tumors are relatively genetically stable

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1 Kuhn E, et al. Ovarian cancer is an imported disease: fact or fiction? *Curr. Obstet. Gynecol. Rep.* 2012; 1(1):1–9 (citing Seidman, JD, et al. Surface epithelial tumors of the ovary. In: Kurman, RJ.; Ellenson, LH.; Ronnett, BM., editors. Blaustein's Pathology of the Female Genital Tract. New York: Springer Verlag; 2011. pp. 679-784).

2 Kuhn E, et al. (2012) (citing Shih IM, Kurman RJ. Ovarian tumorigenesis: a proposed model based on morphological and molecular genetic analysis. *Am J Pathol.* 2004; 164;1511-1518).

3 Kurman RJ, Shih I-M. Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer--shifting the paradigm. *Hum. Pathol.* 2011;42(7):918-931.

4 Kurman RJ, Shih I-M. The Dualistic Model of Ovarian Carcinogenesis. Revisited, Revised and Expanded. *Am. J. Pathol.* 2016;186:733-747.

5 Kurman RJ, Shih I-M (2016).

6 Kuhn E, et al. (2012).

7 Kurman RJ, Shih I-M (2011).

8 Kurman RJ, Shih I-M (2016).

and develop in a stepwise progression from well-established precursor lesions, such as borderline (atypical proliferative) tumors and endometriosis.[9] They typically present as large, unilateral, cystic neoplasms. Except for clear cell carcinomas, which are not graded but are considered high-grade, type I tumors are low-grade. When confined to the ovary, they have an excellent prognosis. Type I tumors account for only 10% of the mortality of ovarian cancer.

Type II tumors are comprised of high-grade serous carcinomas, undifferentiated carcinomas, carcinosarcomas and primary peritoneal carcinomas.[10] Unlike type I tumors, type II tumors are aggressive, present in advanced stage in over 75% of cases, have a very high frequency of *TP53* mutations and show massive genetic instability; they rarely harbor the mutations detected in type I tumors.[11] In addition, type II tumors often have molecular alterations that perturb expression of *BRCA*, either by mutation of the gene or by promotor methylation. Genetic instability is a hallmark of these tumors. Many Type II carcinomas develop from an intraepithelial carcinoma in the fallopian tube and, as a result, disseminate as carcinomas that involve the ovary as well as extraovarian sites, which likely accounts for their clinically aggressive behavior. The volume of tumor in the ovaries (typically both are involved) is substantially less than that of type I tumors, but the volume of extraovarian disease is generally much greater—often with massive disease in the omentum and mesentery. Ascites (fluid in the abdominal/pelvic cavity) frequently accompanies type II tumors but is infrequent with type I tumors.[12] While aggressive surgery and chemotherapy have lengthened survival, type II tumors account for 90% of the mortality of ovarian cancer.[13]

In 2014, the World Health Organization updated the histopathologic classification of ovarian tumors.[14] The morphologic features of these neoplasms are illustrated in the WHO book and in textbooks of gynecologic pathology. For the purposes of this report, I will confine my comments to epithelial ovarian carcinomas (EOCs), which are the focus of the plaintiffs' claims in this litigation. As described herein, the various histological subtypes of EOCs differ in terms of their development (different precursor lesions and genetic mutations involved), clinical course, response to treatment, and pathological findings, as well as associated risk factors. It is hard to imagine that exposure to talcum powder could cause the development of all of these unique histological subtypes of EOC. In fact, even the epidemiology studies that report a weak statistically significant increased risk for talcum powder users have inconsistent results when broken down by histological subtype.

A. Low-Grade Serous Carcinoma

Low-grade serous carcinomas may be noninvasive (niLGSC) or invasive (LGSC). These tumors develop in a stepwise fashion, beginning with a benign proliferative tumor that displays a minimal degree of cytologic atypia (atypical proliferative serous tumor [APST],

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9 Kuhn E, et al. (2012).

10 Kurman RJ, Shih I-M. (2016).

11 Kurman RJ, Shih I-M (2011).

12 Kurman RJ, Shih I-M. (2016).

13 Kurman RJ, Shih I-M. (2016).

14 Kurman RJ, et al. WHO classification of tumours of female reproductive organs. Vol. 6, 4th Ed: IARC, 2014.

also referred to as a serous borderline tumor [SBT]), which progresses to a noninvasive low-grade serous carcinoma (niLGSC) and then to an invasive low-grade serous carcinoma (LGSC). The niLGSC is distinguished from an atypical proliferative serous tumor (APST) or so-called serous borderline tumor (SBT) based on architecture, and more importantly on nuclear features. In contrast to APSTs, niLGSCs have nuclear atypia that is identical to invasive LGSC.[15] Parenthetically, the 2014 WHO Classification regards the term "serous borderline tumor" as synonymous with "atypical proliferative serous tumor," and the term "serous borderline tumor, micropapillary variant" as synonymous with "noninvasive low-grade serous carcinoma."[16] I prefer APST and niLGSC and use these terms in this report.

LGSCs evolve from APSTs in a step-wise fashion and are characterized by sequence mutations in the *KRAS, BRAF* and *ERBB2* oncogenes, which result in constitutive activation of the mitogen-activated protein kinase (MAPK) signal transduction pathway.[17,18,19] Recent studies have implicated a hyperplastic lesion in the fallopian tube designated "papillary tubal hyperplasia" as the precursor of APSTs.[20]

Unlike the other noninvasive tumors, niLGSCs often involve both ovaries and may be associated with extraovarian disease (noninvasive and invasive peritoneal implants) in up to 30% of cases.[21] The mechanisms underlying the development of peritoneal implants have bedeviled investigators for many years. Recently, we have shown that both types of implants have identical *BRAF* or *KRAS* mutation to the ovarian tumors, indicating that they are metastases.[22] Based on this and other findings, the 2014 WHO Classification considers invasive peritoneal implants to be metastatic LGSC.[23]

Following surgery, approximately 10% of APSTs recur as carcinoma, almost always LGSC.[24] Progression to high-grade serous carcinoma (HGSC) occurs very rarely.[25] LGSCs

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15 Kurman RJ, Shih I-M. (2016).

16 Kurman RJ, et al. IARC (2014).

17 Singer G, et al. Mutations in BRAF and KRAS characterize the development of low-grade ovarian serous carcinoma. *J Natl Cancer Inst.* 2003, 95:484-486.

18 Kuo, KT et al. Analysis of DNA copy number alterations in ovarian serous tumors identifies new molecular genetic changes in low-grade and high-grade carcinomas. *Cancer Res.* 2009, 69(9):4036-4042.

19 Pohl G, et al. Inactivation of the mitogen-activated protein kinase pathway as a potential target-based therapy in ovarian serous tumors with KRAS or BRAF mutations. *Cancer Res.* 2005, 65(5):1994-2000.

20 Kurman RJ, et al. Papillary tubal hyperplasia: the putative precursor of ovarian atypical proliferative (borderline) serous tumors, noninvasive implants, and endosalpingiosis. *Am J Surg Pathol.* 2011, 35(11):1605-1614.

21 Kurman RJ, Shih I-M. (2016) (citing Seidman, JD, et al. (2011)).

22 Ardighieri L, et al. Mutational analysis of BRAF and KRAS in ovarian serous borderline (atypical proliferative) tumours and associated peritoneal implants. *J Pathol.* 2014, 232(1):16-22.

23 Kurman RJ, et al. IARC (2014).

24 Kurman RJ, Shih I-M. (2016) (citing Longacre, et al. Ovarian serous tumors of low malignant potential (borderline tumors): outcome-based study of 276 patients with long-term (≥5-year) follow-up. *Am J Surg Pathol*. 2005, 29(6):707-723).

tend to occur in younger women with a mean age of about 50 years. Their clinical course is somewhat variable. In most cases, LGSC are slow-growing tumors characterized by multiple recurrences, but with a survival as long as 20 years. A minority of LGSC behave aggressively, with women succumbing to their disease within a few years after diagnosis. Overall, the mortality of LGSC is 50%. Unlike HGSCs, which initially respond well to cytotoxic chemotherapy, LGSCs are relatively insensitive to this regimen. As a consequence, many gynecologic oncologists follow these women and intervene surgically when symptoms occur.

B. High-Grade Serous Carcinoma

HGSC is the most common and lethal type of ovarian cancer. Recent morphologic, molecular genetic and clinical studies provide evidence that HGSC is more heterogeneous than previously thought.[26,27,28] The Cancer Genome Atlas project (TCGA) analyzed genome-wide sequence mutation, messenger RNA expression, microRNA expression, promoter methylation and DNA copy number in a large number of HGSCs.[29] The results of the TCGA study were largely verified in another genome-wide report.[30] Among the various molecular findings, the most characteristic of HGSC are widespread DNA copy number or structural aberrations and *TP53* mutation. The TCGA project reported that more than 96% of HGSCs have *TP53* mutations; however, a subsequent study by our group demonstrated that, for all practical purposes, *TP53* mutations occur in virtually all HGSCs.[31] In addition to widespread copy number alterations, which reflect the history of genomic instability and ubiquitous *TP53* mutations, other common threads in HGSCs include *CCNE1* amplification, germline and somatic mutation of *BRCA1/2* and other aberrations in pathways regulating homologous recombination DNA damage repair pathways.[32] HGSCs showing *BRCA1/2* deficiency are characterized by more extensive DNA copy number alterations, and usually do not harbor *CCNE1* amplification.[33]

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[25] Dehari R, et al. The development of high-grade serous carcinoma from atypical proliferative (borderline) serous tumors and low-grade micropapillary serous carcinoma: a morphologic and molecular genetic analysis. *Am J Surg Pathol.* 2007, 31(7):1007-1012.

[26] Soslow RA, et al. Morphologic patterns associated with BRCA1 and BRCA2 genotype in ovarian carcinoma. *Mod Pathol.* 2012, 25:625-636.

[27] Howitt BE, et al. Evidence for a dualistic model of high-grade serous carcinoma: BRCA mutation status, histology, and tubal intraepithelial carcinoma. *Am J Surg Pathol.* 2015, 39:287-293.

[28] Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. *Nature* 2011, 474(7353):609-615.

[29] Cancer Genome Atlas Research Network (2011).

[30] Patch AM, et al. Whole-genome characterization of chemoresistant ovarian cancer. *Nature* 2015, 521:489-494.

[31] Vang R, et al. Molecular Alterations of TP53 are a Defining Feature of Ovarian High-Grade Serous Carcinoma: A Rereview of Cases Lacking TP53 Mutations in The Cancer Genome Atlas Ovarian Study. *Int J Gyn Pathol.* 2016;35(1):48–55.

[32] Patch AM, et al. (2015).

[33] Patch AM, et al. (2015).

A gene expression analysis of more than 300 HGSCs identified four molecular subtypes,[34] which were subsequently validated in the TCGA study and termed "immunoreactive," "differentiated," "proliferative," and "mesenchymal" on the basis of gene expression in the clusters.[35] These molecular subtypes have been associated with distinct clinical outcomes.[36,37] In one study, it was shown that survival differed significantly between the subtypes and was best for the immunoreactive subtype,[38] a finding consistent with the histopathological observation that HGSCs with large numbers of tumor-infiltrating lymphocytes are associated with a better outcome. It is postulated that these subtypes may reflect distinct patterns of oncogene activation and that high-grade serous carcinogenesis is initiated by disruption of DNA repair followed by chromosomal instability, copy number change and segregation into molecular subtypes.

Precursor Lesions: Morphologic and Molecular Features. Our understanding of the pathogenesis of ovarian cancer has advanced in the last few years with the recognition that many HGSCs develop from a precursor lesion in the fallopian tube, designated "serous tubal intraepithelial carcinoma (STIC)." This finding was first described in women at high risk of developing ovarian cancer or who had *BRCA* germline mutations, when they underwent risk-reducing salpingo-oophorectomy (RRSO, resection of the ovaries and fallopian tubes).[39,40,41,42] Subsequently, STICs were detected in 50-60% of women with sporadic HGSC.[43] STICs are detected in the absence of an ovarian carcinoma in approximately 5% of women at high risk who are undergoing risk reducing salpingo-oophorectomy, as noted above. More recently, incidental STICs have been reported in women undergoing hysterectomy and bilateral salpingo-oophorectomy for non-prophylactic reasons, who were not known to have *BRCA* mutations in both selected[44,45] and unselected series.[46,47,48] Other data supporting STIC as the

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[34] Tothill RW, et al. Novel molecular subtypes of serous and endometrioid ovarian cancer linked to clinical outcome. *Clin Can Res*. 2008, 14:5198-5208.

[35] Cancer Genome Atlas Research Network (2011).

[36] Helland A, et al. Deregulation of MYCN, LIN28B and LET7 in a molecular subtype of aggressive high-grade serous ovarian cancers. *PloS one* 2011, 6:e18064.

[37] Konecny GE, et al. Prognostic and therapeutic relevance of molecular subtypes in high-grade serous ovarian cancer. *J Natl Can Inst*. 2014; 106(10).

[38] Konecny GE, et al. (2014).

[39] Piek JM, et al. Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. *J Pathol.* 2001, 195(4):451-456.

[40] Piek JM, et al. Tubal ligation and risk of ovarian cancer. *Lancet* 2001, 358(9284):844.

[41] Piek JM, et al. BRCA1/2-related ovarian cancers are of tubal origin: a hypothesis. *Gynecol Oncol*. 2003, 90(2):491.

[42] Finch A, et al. Salpingo-oophorectomy and the risk of ovarian, fallopian tube, and peritoneal cancers in women with a BRCA1 or BRCA2 Mutation. *JAMA* 2006, 296:185-192.

[43] Kurman RJ, Shih I-M. (2016) (citing Kindelberger DW, et al. Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: Evidence for a causal relationship. *Am J Surg Pathol.* 2007, 31(2):161-169; Przybycin CG, et al. Are all pelvic (nonuterine) serous carcinomas of tubal origin? *Am J Surg Pathol.* 2010, 34(1):1407-1416).

[44] Morrison JC, et al. Incidental serous tubal intraepithelial carcinoma and early invasive serous carcinoma in the nonprophylactic setting: analysis of a case series. *Am J Surg Pathol.* 2015, 39(4):442-453.

precursor lesion to HGSC include findings of identical *TP53* mutations in women with concomitant STIC and HGSC of the ovary, supporting the clonal relationship of the two lesions. Parenthetically, *TP53* mutation appears to be the earliest genetic alteration that occurs in the development of HGSC. Also, STIC, as compared to the concomitant ovarian tumor, have shorter telomeres, and shortened telomeres are one of the earliest molecular changes in carcinogenesis. Finally, in molecularly engineered mouse models, inactivation of *BRCA*, *TP53* and *PTEN* leads to the development of STICs and ovarian HGSC.[49] When salpingectomy is performed at an early age, no cancers develop, whereas neither oophorectomy nor hysterectomy prevents the development of cancer.[50] A recent epidemiologic study showed that in women who had prior salpingectomy, the risk of developing HGSC was significantly decreased as compared to that of women with intact fallopian tubes, further supporting the tubal origin of HGSC.[51]

C. Endometrioid Carcinoma

The great majority of endometrioid carcinomas are well differentiated, but occasionally, moderately and poorly differentiated carcinomas are observed. The frequent finding of well differentiated areas in the moderately and poorly differentiated neoplasms suggests that the latter "de-differentiated" from low-grade carcinomas. Activating mutations of *CTNNB1* occur in roughly 15-40% of ovarian endometrioid carcinomas, and mutation of this gene is associated with squamous differentiation, low tumor grade and favorable outcome.[52] In addition, inactivating mutations in *PTEN* have been reported in 15%-20% of

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[45] Gilks CB, et al. Incidental nonuterine high-grade serous carcinomas arise in the fallopian tube in most cases: further evidence for the tubal origin of high-grade serous carcinomas. *Am J Surg Pathol.* 2015, 39:357-364.

[46] Hirst JE, et al. High rates of occult fallopian tube cancer diagnosed at prophylactic bilateral salpingo-oophorectomy. *Int J Gyn Can.* 2009, 19(5):826-829.

[47] Rabban JT, et al. Early detection of high-grade tubal serous carcinoma in women at low risk for hereditary breast and ovarian cancer syndrome by systematic examination of fallopian tubes incidentally removed during benign surgery. *Am J Surg Pathol.* 2014, 38(6):729-742.

[48] Tang S, et al. Frequency of serous tubal intraepithelial carcinoma in various gynecologic malignancies: a study of 300 consecutive cases. *Int J Gyn Pathol.* 2012, 31(2):103-110.

[49] Kurman RJ, Shih I-M. (2016).

[50] Perets R, et al. Transformation of the fallopian tube secretory epithelium leads to high-grade serous ovarian cancer in Brca;Tp53;Pten models. *Can Cell.* 2013, 24:751-765.

[51] Kurman RJ, Shih I-M. (2016) (citing Falconer H, et al. Ovarian cancer risk after salpingectomy: a nationwide population-based study. *J Natl Can Inst.* 2015, 107(2); McAlpine JN, et al. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. *Am J Ob Gyn.* 2014, 210:471 e1-11).

[52] Kurman RJ, Shih I-M. (2016) (citing Wu R, et al. Mouse model of human ovarian endometrioid adenocarcinoma based on somatic defects in the Wnt/beta-catenin and PI3K/Pten signaling pathways. *Cancer Cell.* 2007; 11:321–333; Saegusa M, et al. P-Catenin mutations and aberrant nuclear expression during endometrial tumorigenesis. *Br. J. Cancer.* 2001; 84:209-217).

endometrioid carcinomas and activating mutations of *PIK3CA* occur in 20% of these tumors.[53] These genes are rarely mutated in other types of ovarian cancer.

Morphologic and molecular studies provide cogent evidence that ovarian endometrioid carcinoma is derived from endometriosis and therefore endometriosis is regarded as a precursor lesion. Endometriosis is composed of ectopic endometrial tissue that resembles the endometrium lining the uterine cavity and simulates the normal endometrium by periodically bleeding (menstruating). The first study describing the association of endometriosis with ovarian carcinoma was published in 1927.[54] Over the years, this has become well accepted, being cited in numerous textbooks of gynecologic pathology, including the first edition of Blaustein's Pathology of the Female Genital tract published in 1977 and subsequent editions, as well as in the AFIP Fascicle on Tumors of the Ovary published in 1979[55] and most recently in the 7th edition of Blaustein's Pathology of the Female Genital Tract (in press) and the WHO Classification of Tumours of the Female Reproductive Organs, published in 2014. The older studies were based on clinical and histopathologic observations demonstrating a morphologic continuum from benign endometriosis to atypical endometriosis, which merged imperceptibly into endometrioid and clear cell carcinomas in many cases.[56,57] These findings have been confirmed by recent molecular genetic studies. Specifically, somatic mutations of *ARID1A*, a tumor suppressor gene involved in chromatin remodeling,[58] have recently been reported in a large proportion of endometrioid-related neoplasms, including 30% of ovarian endometrioid carcinomas[59] and 46-57% of ovarian clear cell carcinomas.[60] These mutations are rarely reported (< 10%) in other types of ovarian carcinomas.[61] Importantly, mutation and loss of expression of this gene have been found in the endometriotic epithelium in

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[53] Kurman RJ, Shih I-M. (2016) (citing Catasus L, Bussagalia, E, et al. Molecular genetic alterations in endometrioid carcinomas of the ovary: similar frequency of beta-catenin abnormalities but lower rate of microsatellite instability and PTEN alterations than in uterine endometrioid carcinomas. *Hum. Pathol.* 2004; 35:1360-1368; Nakayama K, et al. Sequence mutations and amplification of PIK3CA and AKT2 genes in purified ovarian serous neoplasms. *Cancer Biol. Ther.* 2006;5:779-785).

[54] Kuhn E, et al. (2012) (citing Sampson JA. Metastatic or embolic endometriosis, due to the menstrual dissemination of endometrial tissue into the venous circulation. *Am J Pathol.* 1927; 3(2):93-110.43).

[55] Scully RE. Tumors of the Ovary and Maldeveloped Gonads. Atlas of Tumor Pathology, Second Series, Fascicle 16, Armed Forces Institute of Pathology, Washington D.C., 1979.

[56] Fukunaga M, et al. Ovarian atypical endometriosis: its close association with malignant epithelial tumours. *Histopathol.* 1997; 30(3):249-255.

[57] Russell P. The pathological assessment of ovarian neoplasms. I: Introduction to the common 'epithelial' tumours and analysis of benign 'epithelial' tumours. *Pathol*. 1979; 11(1):5-26.

[58] Kuhn E, et al. (2012) (citing Guan B, et al. ARID1A, a factor that promotes formation of SWI/SNF-mediated chromatin remodeling, is a tumor suppressor in gynecologic cancers. *Cancer Res.* 2011; 71(21):6718-6727).

[59] Kuhn E, et al. (2012) (citing Wiegand KC, et al. ARID1A mutations in endometriosis-associated ovarian carcinomas. *N. Engl. J. Med.* 2010; 363(16):1532-1543).

[60] Kuhn E, et al. (2012) (citing Jones S, et al. Frequent mutations of chromatin remodeling gene ARID1A in ovarian clear cell carcinoma. *Science.* 2010; 330:228-231; Wiegand KC, et al. (2010)).

[61] Kuhn E, et al. (2012) (citing Jones S, et al. Somatic mutations in the chromatin remodeling gene ARID1A occur in several tumor types. *Hum. Mutat.* 2011 Oct 18. Published in print: 2012;33(1):100-103).

endometriomas immediately adjacent to ovarian endometrioid carcinomas.[62] Somatic mutations of *PTEN* have also been demonstrated in endometrioid and clear cell carcinomas and in endometriotic cysts. These molecular genetic findings provide compelling evidence that endometriosis and endometriotic cysts are precursors of these neoplasms.[63]

Endometrioid carcinomas are frequently associated with endometriotic cysts, and approximately 40% are associated with endometriosis elsewhere in the pelvis.[64] Patients with endometriosis are approximately 2-4 times more likely to develop ovarian endometrioid carcinoma.[65] The precise origin of endometriosis has not been conclusively established; proposed mechanisms include retrograde menstrual flow and in situ development in the peritoneum through a process of metaplasia. Other mechanisms, including development from embryonic rests, have also been invoked. Most cases are best accounted for by retrograde menstruation (endometrial tissue expelled at the time of menstruation, which passes through the fallopian tubes and implants on the ovary and other sites in the peritoneal cavity). Of significance is the observation that eutopic endometrium (the endometrial tissue within the uterus) of women with endometriosis displays intrinsic molecular abnormalities, including activation of oncogenic pathways, that are not found in the eutopic endometrium of women without endometriosis.[66] This suggests that endometriosis develops from retrograde endometrial tissue, which has these molecular abnormalities, thereby permitting the endometrial tissue to implant and possibly undergo malignant transformation outside the uterus.[67] Also supportive of this hypothesis are epidemiologic data that indicate the protective effect for tubal ligation is stronger for endometrioid and clear cell carcinoma than for HGSC, presumably because tubal ligation interrupts the retrograde passage of endometrial tissue from the uterus to the peritoneal cavity.[68] However, this mechanism does not fit well with the development of HGSC, which is now thought to derive from a precursor lesion in the fimbriated end (the most distal portion) of the fallopian tube, which is in close contact with the ovary. Importantly, Tiourin, et al. demonstrated in humans and mouse models "that tubal ligation induces quiescence of distal fallopian tube epithelium" by decreasing the number and

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62 Kurman RJ, Shih I-M. (2016) (citing Wiegand KC, et al. (2010)); Ayhan A, et al. Loss of ARID1A expression is an early molecular event in tumor progression from ovarian endometriotic cyst to clear cell and endometrioid carcinoma. *Int J Gynecol Cancer*. 2012, 22:1310-1315).

63 Kurman RJ, Shih I-M (2016) (citing Sato N, et al. Loss of heterozygosity on 10q23.3 and mutation of the tumor suppressor gene PTEN in benign endometrial cyst of the ovary: possible sequence progression from benign endometrial cyst to endometrioid carcinoma and clear cell carcinoma of the ovary. *Cancer Res.* 2000, 60:7052-7056).

64 Kuhn E, et al. (2012) (citing Veras E, et al. Cystic and adenofibromatous clear cell carcinomas of the ovary: distinctive tumors that differ in their pathogenesis and behavior: a clinicopathologic analysis of 122 cases. *Am. J. Surg. Pathol.* 2009; 33:844-853).

65 Kuhn E, et al. (2012) (citing Kokcu A. Relationship between endometriosis and cancer from current perspective. *Arch. Gynecol. Obstet.* 2011; 284(6):1473-1479).

66 Kurman RJ, Shih I-M (2011) (citing Bulun SE. Endometriosis. *N. Engl. J. Med.* 2009; 360(3):268-279).

67 Kurman RJ, Shih I-M (2011) (citing Bulun SE. (2009)).

68 Rosenblatt KA, et al. Reduced risk of ovarian cancer in women with a tubal ligation or hysterectomy. The World Health Organization Collaborative Study of Neoplasia and Steroid Contraceptives. *Cancer Epidemiol. Biomarkers Prev.* 1996; 5(11):933-935.

proliferation of progenitor cells in that region, which can explain the slight reduction in the risk of HGSC associated with this procedure.[69]

Cancer is a genetic disease, driven by changes to DNA that alter normal cellular functions, and therefore the most powerful evidence relating to the histogenesis of cancer is based on molecular genetic findings. The shared molecular genetic findings between endometriosis and endometrioid carcinoma are particularly compelling in support of endometriosis as the precursor of endometrioid carcinoma. Accordingly, when endometriosis is found in the overall specimen, pathologists regard this as ample evidence of an origin from endometriosis, even in the absence of a demonstrable transition from endometriosis to the tumor.

D. Clear Cell Carcinoma

In contrast to the other type I tumors, clear cell carcinomas are not graded. They are generally regarded as high grade, unlike the other type I tumors. Occasionally, both endometrioid and clear cell carcinoma components coexist in an ovarian tumor. Somatic inactivating mutations of *ARID1A* occur in about 50% of clear cell carcinomas,[70] while activating mutations of *PIK3CA* occur in 20%,[71] *PTEN* in almost 10%[72,73] and roughly 3% in the catenin gene (*CTNNB1* encodes b-catenin).[74] These genes are rarely mutated in other types of ovarian cancer.[75] The precursor lesion for clear cell carcinoma, like endometrioid carcinoma, is endometriosis.

E. Seromucinous Carcinomas (Mixed Müllerian Carcinomas)

Most seromucinous carcinomas are noninvasive. They are generally papillary and resemble niLGSCs but, in fact, are composed of a mixture of epithelial cell types, including endometrioid and squamous cells and endocervical-type mucinous cells. Furthermore, their immunoprofile is characterized by frequent expression of estrogen receptor (ER) (100%), progesterone receptor (PR) (67%), and cancer antigen 125 (CA125; 92%); infrequent expression of WT1 (8%); and lack of expression of cytokeratin 20 (CK20) and caudal type homeobox 2 (CDX2). This immunostaining pattern is consistent with a Müllerian immunophenotype. Loss of ARID1A expression was reported in one-third of cases,[76] which is

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[69] Tiourin E, et al. Tubal ligation induces quiescence in the epithelia of the fallopian tube fimbria. *Reprod Sci*. 2015;22(10):1262-1271.

[70] Kurman RJ, Shih I-M. (2016) (citing Jones S, et al. (2010); Wiegand, et al. (2010); Ayhan A, et al. (2012)).

[71] Kurman RJ, Shih I-M. (2016) (citing Nakayama K, et al. (2006); Jones S, et al. (2010)).

[72] Kurman RJ, Shih I-M. (2016).

[73] Sato N, et al. (2000).

[74] Kuo K-T, et al. Frequent activating mutations of PIK3CA in ovarian clear cell carcinoma. *Am J Pathol.* 2009;174(5):1597-1601.

[75] Kurman RJ, Shih I-M (2016).

[76] Wu CH, et al. Endocervical-type mucinous borderline tumors are related to endometrioid tumors based on mutation and loss of expression of ARID1A. *Int J Gynecol Pathol* 2012;31(4):297-303.

similar to the frequency in endometrioid and clear cell tumors, providing compelling evidence to include them in the group of endometriosis-related neoplasms.

F. Mucinous Carcinoma

Most mucinous carcinomas are well differentiated; moderate and poorly differentiated tumors are relatively uncommon. Typically, mucinous carcinomas are quite heterogeneous, containing areas of cystadenoma and atypical proliferative tumor intimately admixed with areas of carcinoma. A recent study that used next-generation sequencing found that *KRAS*-activating mutation is the most common single molecular genetic alteration in mucinous carcinomas, occurring in 65% of cases.[77] In contrast to other type I ovarian carcinomas, *TP53* mutation is frequent in mucinous carcinomas, being present in approximately one-half of cases.[78] It should be noted that, until recently, mucinous carcinoma was thought to be the second most frequent ovarian carcinoma. However, studies have now shown that the majority of mucinous carcinomas involving the ovary are, in fact, metastases from primary gastrointestinal tract tumors. In fact, Figure 6 on page 43 of the report of plaintiffs' expert Dr. Sarah Kane is an example of a primary mucinous carcinoma of the gastrointestinal tract that metastasized to the ovary. Based on my experience with these tumors, it most likely originated from the appendix.[79,80,81,82] In her report, Dr. Kane incorrectly identifies this tumor as a primary mucinous carcinoma of the ovary.

G. Malignant Brenner Tumors

These tumors are composed of nests of transitional-type epithelium surrounded by a fibromatous stroma. Typically, the nests of transitional epithelium have a central cystic cavity lined by mucinous epithelium. Most Brenner tumors are benign, less commonly atypical proliferative, and rarely malignant; consequently, a comprehensive molecular analysis of malignant Brenner tumors has not been performed.

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77 Mackenzie, R, et al. Targeted deep sequencing of mucinous ovarian tumors reveals multiple overlapping RAS-pathway activating mutations in borderline and cancerous neoplasms. *BMC Cancer*. 2015;15:415.

78 Mackenzie, R, et al. (2015).

79 Shappell H, et al. Diagnostic criteria and behavior of seromucinous (endocervical-type mucinous and mixed cell-type) tumors. *Am J Surg Pathol*. 2002:26(12):1529-1541.

80 Ronnett BM, et al. Patients with pseudomyxoma peritonei associated with disseminated peritoneal adenomucinosis have a significantly more favorable prognosis than patients with peritoneal mucinous carcinomatosis. *Cancer*. 2001;92(1):85-91.

81 Ronnett BM, et al. Pseudomyxoma peritonei in women: A clinicopathologic analysis of 30 cases with emphasis on site of origin, prognosis, and relationship to ovarian mucinous tumors of low malignant potential. *Hum Pathol*. 1995;26(5):509-524.

82 Seidman JD, et al. Primary and metastatic mucinous adenocarcinomas in the ovaries: incidence in routine practice with a new approach to improve intraoperative diagnosis. *Am J Surg Pathol*. 2003; 27(7):985-993.

II. DR. SARAH KANE'S EXPERT REPORT

Dr. Kane is the only pathologist designated on behalf of the plaintiffs. She has produced a lengthy report, but only a single paragraph addresses ovarian cancer pathology.[83] Dr. Kane opines that "genital talcum powder exposure can cause ovarian cancer" based on her evaluation of "epidemiological . . ., pathological, biological, and mechanistic evidence."[84] Although Dr. Kane offers opinions in a host of areas outside her field, including epidemiology and cancer biology, I will focus my report on my primary area of expertise: gynecologic pathology.

Based on my nearly 40 years of experience researching the pathogenesis of ovarian cancer, I have concluded that Dr. Kane's opinions reflect a misunderstanding of ovarian cancer pathology, are highly speculative and are contrary to sound science.

Like all cancers, ovarian carcinomas are driven by changes to DNA that alter normal cellular functions. These molecular genetic alterations are the most powerful evidence relating to ovarian cancer development. As described more fully in section I and Appendix I of my report, epithelial ovarian cancer comprises distinctly different carcinomas (i.e., high-grade serous, low-grade serous, endometrioid, clear cell, seromucinous, mucinous and malignant Brenner tumors), each with different precursor lesions, morphologies, clinical behaviors, pathogenesis, and molecular genetic alterations. Dr. Kane does not identify any studies linking the use of talc-based body powders to the known genetic alterations associated with the various histologic subtypes of ovarian cancer. And indeed, I am aware of no such studies. Further, it is unlikely that exposure to a single agent, i.e., talc, could result in the development of such distinctly different neoplasms. Finally, ovarian carcinomas differ dramatically from mesothelioma, and Dr. Kane's repeated efforts to analogize ovarian cancer to mesothelioma are both unscientific and misleading.

Below I focus on four opinions by Dr. Kane that are unsupported by, and contrary to, the current data and understanding of ovarian cancer pathology: (1) that "similarities" between talc and asbestos and between HGSC and mesothelioma support the conclusion that talc causes ovarian cancer; (2) that talc use causes ovarian cancer through inflammation; (3) that reported observations of talc in pathology samples are "consistent with causation"; and (4) that talcum powder applied to the external perineum can migrate to the ovaries.

A. "Similarities" Between Talc and Asbestos and Between HGSC and Mesothelioma

One of the major premises Dr. Kane relies on to support her causation opinion is the notion that because talc is supposedly chemically similar to asbestos (which causes mesothelioma) and because HGSC is similar to mesothelioma, there is support for her

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[83] It appears Dr. Kane may have initially prepared a report that included more expansive opinions on pathology that were removed or deleted during the drafting process. When I reviewed her deposition, I noted that she was asked to identify where in her report she addressed ovarian cancer pathogenesis and she stated that she "did the work," but could not "discuss it because of attorney work product issues." January 25, 2019 Deposition of Dr. Kane ("Kane Deposition"), pages 206-213.

[84] November 15, 2018 Report of Dr. Kane ("Kane Report") at 37.

opinion that talc use causes ovarian cancer.[85] Dr. Kane attempts to support this argument by pointing to "the chemical similarity between asbestos and talc" and "morphologic and immunohistochemical similarities" between mesothelioma and HGSC.[86] Relatedly, Dr. Kane reports that she has seen evidence that talcum powder products contain asbestos and discusses epidemiological studies assessing asbestos exposure and ovarian cancer, which she claims further support her opinion that talc use causes ovarian cancer.[87] She also claims that the similarities she observes between talc and asbestos and between HGSC and mesothelioma support the "analogy" criterion of Bradford Hill.[88] Dr. Kane's analysis is methodologically flawed and lacks a sound scientific basis.

First, Dr. Kane overstates the significance of compositional similarities between talc and asbestos. Specifically, Dr. Kane relies on an observed "chemical similarity" between the two.[89] But the fact that two materials have similar chemical compositions does not mean they will have similar effects on the body. For instance, the chemical composition of water (H_2O) is almost identical to that of hydrogen peroxide (H_2O_2)—they differ by only one oxygen atom—but their biological effects are vastly different. Dr. Kane fails to provide any support for her suggestion that compositional similarities between talc and asbestos result in similar biologic effects. While talc and asbestos are both silicate minerals, talc is inert; by contrast, surface reactivity and the ability to release free radicals contribute to the pathogenic effects of asbestos.[90]

Second, Dr. Kane downplays the importance and extent of the structural differences between talc and asbestos, noting only that they are "*somewhat* morphologically distinct."[91] The structure of substances can be extremely important in their functional activity in the body. According to IARC, "talc particles are normally plate-like" and are stable and inert.[92] By contrast, asbestos occurs in bundles of flexible, needle-shaped fibers. The effects of asbestos on the body are determined by, among other things, the geometry and surface reactivity of the fibers.[93] Dr. Kane fails to acknowledge these critical structural differences in her attempt to analogize talc to asbestos.

Relatedly, Dr. Kane's assessment of studies examining the association between asbestos exposure and ovarian cancer is not analytically sound.[94] As an initial matter, because

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85 Kane Report at 13-14.

86 Kane Report at 5, 14.

87 Kane Report at 29-33.

88 Kane Report at 37.

89 Kane Report at 5, 13.

90 International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans, volume 100C. Arsenic, Metals, Fibres and Dusts*; 1.6, 4.3. Lyon, France: IARC; 2012 ("IARC Monograph").

91 Kane Report at 13.

92 IARC Monograph at 1.6.

93 IARC Monograph at 4.3.

94 Kane Report at 29-33.

talc and asbestos are distinct minerals, as explained above, Dr. Kane's discussion of these studies is not relevant to whether perineal talc use causes ovarian cancer. (As Dr. Kane does not provide any description or analysis of the "evidence" she has seen that talcum products contain asbestos[95] and testified that her opinion "is not dependent on asbestos being in the product,"[96] I will not evaluate that assertion here.) In any event, although it is well established that asbestos exposure can cause pleural mesothelioma (and much less commonly lung cancer), the data implicating asbestos exposure and ovarian cancer is significantly weaker. The studies Dr. Kane discusses – which reported only a handful of ovarian cancer cases – involved significant exposure to industrial asbestos sustained via inhalation by women who worked in occupations where they were regularly exposed to asbestos for hours every day (such as in factories producing gas masks). These studies of occupational asbestos exposures are not directly applicable to **perineal** application of cosmetic talcum powder, which is the exposure alleged in these cases. Dr. Kane fails to explain how perineal exposure to alleged contaminant levels of asbestos in cosmetic talc is similar to occupational exposures to inhaled industrial asbestos. Finally, from a pathology standpoint, there is a significant likelihood that some tumors observed in these occupational studies, which are quite dated, were misclassified due to misreporting on death certificates and lack of immunohistochemical analysis to adequately distinguish peritoneal mesothelioma from ovarian cancer (i.e., peritoneal mesotheliomas were misdiagnosed as ovarian carcinomas).[97,98]

Dr. Kane's claim that similarities between HGSC and mesothelioma support her conclusion that talc causes ovarian cancer also fails to account for decades of important research on ovarian cancer pathogenesis. For one thing, Dr. Kane grossly overstates the "striking morphologic similarities" between HGSC and mesothelioma. These "striking similarities" she claims to observe are supported by Figures 1 and 2 of her report, which are photomicrographs of tumors taken at a very high magnification. It is impossible to appreciate the differences between two tumors when they are viewed at such a high magnification. In practice, it is relatively straightforward for an experienced gynecologic pathologist to distinguish between HGSC and mesothelioma by morphology on routine microscopic analysis. While there is some overlap between the immunohistochemical markers expressed by mesotheliomas and HGSC,[99] this is true of many different tumors and does not support Dr. Kane's suggestion that mesothelioma and HGSC are similar diseases.. Moreover, Dr. Kane is mistaken when she claims that calretinin is a common marker expressed by HGSC and mesotheliomas. In fact, calretinin is rarely expressed by serous carcinomas, but is expressed in the majority of mesotheliomas; therefore, it is actually used to differentiate mesothelioma from serous carcinoma. Other immunohistochemical markers used to differentiate serous ovarian carcinomas from mesotheliomas include MOC31, PAX8, Claudin4, BER-EP4 and

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95 Kane Report at 29.

96 Kane Deposition, page 227.

97 Reid, et al. Does Exposure to Asbestos Cause Ovarian Cancer: A Systemic Literature Review and Meta-Analysis. *Cancer Epidemiol Biomarkers Prev*. 2011; 20(7):1287-1295.

98 Camargo, et al. Occupational Exposure to Asbestos Ovarian Cancer: A Meta-Analysis. *Environ Health Perspect* 2011; 119(9): 1212-1217 (evaluates effect of misclassification by removing 20% of ovarian cancer cases from every study and repeating meta-analysis).

99 Kane Report at 14.

Estrogen Receptor.[100] There is substantial evidence now that HGSC derives from the Mullerian epithelium of the fallopian tube, and not from the modified mesothelium that lines the ovaries – another important distinction between these tumors.[101]

Finally, I note that the morphologic and molecular genetic differences between mesothelioma and the other types of epithelial ovarian carcinoma, specifically, low-grade serous, endometrioid, clear cell, and mucinous carcinomas and malignant Brenner tumors, is even more stark than those of HGSC. In particular, endometrioid and clear cell carcinoma develop from endometriosis (which is a precursor lesion to these cancers, as explained previously). Endometriosis is composed of endometrial type cells, which are also of Mullerian origin and resemble cells lining the uterine cavity – cells that are likewise significantly different from mesothelial cells.

In summary, Dr. Kane inappropriately overstates the similarities between talc and asbestos and HGSC and mesothelioma, and fails to appreciate the important differences between these minerals and diseases. When applied to the "analogy" criterion of her Bradford Hill analysis, these inaccuracies and overstatements undermine her conclusions.[102]

B. Talc-Induced Chronic Inflammation as a Cause of Ovarian Cancer

Dr. Kane's report includes a lengthy discussion setting forth her view that perineal use of talc causes chronic inflammation that leads to cancer.[103] These speculative opinions are not supported by sound science. As explained further below, while it is true that talc can elicit an inflammatory response in tissue, the type of response associated with talc is what pathologists refer to as a "foreign body response" or "foreign body granuloma." Foreign body granulomas have only rarely been reported in gynecologic pathology samples and they have not been associated with the perineal use of talcum powder.

As a preliminary matter, it is important to clearly define "chronic inflammation" and differentiate between the different types of chronic inflammation. Generally, inflammation can be defined as "a protective response elicited by injury or destruction of tissues which serves to destroy, dilute or wall off the injurious agent and the injured tissue."[104] If the inflammatory reaction persists for an extended period, it is referred to as "chronic" inflammation.

The different types of chronic inflammation have different histologic appearances. The most common type is composed of a variety of inflammatory cells, including lymphocytes, plasma cells and histiocytes (macrophages).[105] A less frequently encountered

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100 Husain AN, et al. Guidelines for Pathologic Diagnosis of Malignant Mesothelioma. *Arch Pathol Lab Med.* 2018; 142:89-108.

101 Kurman RJ, Shih I-M. (2016).

102 Kane Report at 37.

103 Kane Report at 9-13.

104 Dorland, W A. N., Dorland's Illustrated Medical Dictionary. Philadelphia, PA: Saunders.

105 Dr. Kane suggests that lymphocytes and plasma cells are a marker of carcinogenesis. Kane Deposition, pages 58, 63, 98-99, 108. This is not correct. Plasma cells and lymphocytes are not markers for cancer.

type of chronic inflammation – granulomatous inflammation – is characterized by focal lesions, called granulomas. Granulomas can be divided into two broad categories: (1) immune granulomas and (2) foreign body granulomas.[106, 107] Foreign-body granulomas are what you would expect to find in tissue exposed to noninfectious material, like talc and surgical sutures.[108] The reaction is characterized by an inflammatory infiltrate composed predominantly of histiocytes, which may fuse to form giant cells that surround and phagocytose material. Notably, I have examined a number of surgical pathology specimens from plaintiffs in talc litigation and have not observed foreign body granulomas or foreign body granulomatous inflammation associated with alleged talc use. Indeed, in the course of my 40 years of looking at microscopic slides of ovarian cancer, I have only seen foreign body granulomatous inflammation associated with ovarian tumors very rarely. The associated tumors have been predominantly teratomas (which are not epithelial carcinomas); less than a handful were endometrioid carcinomas. In all these cases, the granulomatous inflammation was in response to keratin produced by the tumor and had nothing to do with talc (no evidence of polarized crystals that may have been talc).

Dr. Kane was unable to identify the frequency with which she observed foreign body granulomatous inflammation, much less foreign body granulomas, in the gynecological specimens that she has examined throughout her career.[109] Of the granulomas she has observed, Dr. Kane was unable to testify that any were foreign body talc granulomas, because she does not routinely use polarized light microscopy to look for particulates in gynecologic tissue.[110] Dr. Kane attempts to compensate for the general lack of histologic evidence supporting biologic talc exposure by speculating about the latency period between the onset of inflammation and development of cancer.[111] However, the majority of women who use talc begin their use around age 20 and that use is habitual.[112] In other words, it appears that for most cases, the exposure and, therefore, the resulting inflammation, would not be remote but continuous.

Dr. Kane points to the association between endometriosis and the development of endometrioid and clear cell carcinoma as evidence that chronic inflammation causes ovarian cancer.[113] Her conclusions are based on speculation rather than data. Chronic inflammation has not been proven to be the mechanism by which endometriosis develops into endometrioid and clear cell carcinomas. In fact, endometriosis is often not accompanied by inflammation, and when it is, the inflammation is composed of lymphocytes and plasma cells, not foreign

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106 Shah KK, et al. Histopathologic Review of Granulomatous Inflammation. *J Clin Tuberculosis Micobacterial Dis.* 2017;7:1-12.

107 deBrito T and Franco MF. Viewpoint: Granulomatous Inflammation. *Rev Inst Med trop Sao Paulo.* 1994;36(2):185-192.

108 Shah KK, et al. (2017).

109 Kane Deposition, pages 110, 115-16.

110 Kane Deposition, pages 108-09.

111 Kane Report at 12.

112 Cramer DW, et al. The Association Between Talc Use and Ovarian Cancer: A Retrospective Case-Control Study in Two US States. *Epidemiol.* 2016(3);27:334-346.

113 Kane Report at 10, 12.

body granulomatous reactions like those associated with talc exposure. Moreover, based on the fact that shared molecular genetic changes have been found in endometriosis and endometrioid and clear cell carcinoma, the scientific evidence strongly suggests that endometriosis is a precursor lesion to these cancers, not a source of inflammation that causes them. Significantly, in women with endometriosis, the eutopic endometrium (endometrium lining the uterine cavity) displays molecular changes that are not present in the eutopic endometrium of women without endometriosis, suggesting that the abnormalities found in the endometrium are predisposing to both the development of endometriosis and endometrioid carcinoma.[114]

Dr. Kane similarly cites pelvic inflammatory disease (PID) as evidence that chronic inflammation causes ovarian cancer.[115] However, the association between PID and ovarian cancer has been inconsistent. It appears to be limited to serous borderline tumors and possibly LGSC.[116] As described in Section I, LGSC and HGSC are very different diseases and develop along different molecular genetic pathways.

In another attempt to analogize talc to asbestos, Dr. Kane cites talc's use in pleurodesis – a procedure in which talc is injected into the pleural space to treat benign recurrent pneumothorax or pleural effusion – to suggest that the consequences of talc-induced inflammation are similar to those of asbestos-induced inflammation.[117] While both talc particles and asbestos fibers can cause chronic inflammation and fibrosis, inflammation and fibrosis are natural responses to a variety of stimuli and are not specific to talc, asbestos or even the cancer process. Further, if the consequences of talc and asbestos exposure were similar (e.g., if both caused cancer), one would expect to find cancer arising in patients who underwent talc pleurodesis. On the contrary, based on my review of the literature, talc pleurodesis has not been associated with the development of cancer, including mesothelioma, in patients followed for up to 40 years.[118,119] In fact, some studies of talc as a treatment for malignant pleural effusion suggest it may have anti-tumorigenic effects, promoting apoptosis (programmed cell death) in malignant mesothelioma cells[120] and inhibiting tumor progression by promoting angiostasis.[121] Defective apoptotic signaling pathways and inhibition of angiostasis play an important role in the initiation and progression of cancer and are related to tumor aggressiveness and survival.

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114 Kurman RJ, Shih I-M (2011) (citing Bulun SE. (1999)).

115 Kane Report at 10, 12.

116 Rasmussen CB, et al. Pelvic Inflammatory Disease and the Risk of Ovarian Cancer and Borderline Ovarian Tumors: A Pooled Analysis of 13 Case-Control Studies. *Am J Epidemiol*. 2017;185(1):8-20.

117 Kane Report at 13.

118 Hunt, et al. Is talc pleurodesis safe for young patients following primary spontaneous pneumothorax? *Interactive CardioVascular and Thoracic Surgery*. 2007; 6(1):117-120.

119 Light RW Letter to Editor in Ghio AJ, et al. *Am J Respir Crit Care Med*. 2001;164:1741.

120 Nasreen N, et al. Talc Induces Apoptosis in Human Malignant Mesothelioma Cells *In Vitro*. *Am J Respir Crit Care Med.* 2000;161:595-600.

121 Nasreen N, et al. Talc mediates angiostasis in malignant pleural effusions *via* endostatin production. *Eur Respir J.* 2007;29:761-769.

Further, if chronic inflammation plays a key role in the development of HGSC, the most common ovarian malignancy, one would expect to find evidence of inflammation associated with early precursor lesions. It is now widely accepted that STICs (serous tubal intraepithelial carcinoma) are confined to the tubal epithelium; in other words, they have not invaded normal tissue. STICs are considered the immediate precursor of invasive HGSC. I have participated in a number of studies assessing the characteristics of STICs and have not found them to be associated with inflammation. Others have reported similar observations.[122] Recent data suggest that an even earlier lesion, designated "p53 signature," which is characterized by normal appearing fallopian tube epithelium but harboring a *TP53* mutation, is the precursor of STICs. I have not seen inflammation associated with p53 signatures in the fallopian tube.

Finally, many of the studies that Dr. Kane cites to attempt to show how chronic inflammation can lead to the development of cancer are not relevant to talc-associated foreign body reactions. In particular, Dr. Kane's use of ulcerative colitis – a type of inflammatory bowel disease that is associated with an increased risk of colon cancer – as a surrogate for talc causing ovarian cancer[123] is highly misleading because it fails to distinguish the chronic inflammation associated with ulcerative colitis from the foreign body response association with talc exposure. The former is characterized by the presence of neutrophils, lymphocytes and plasma cells accompanied by features of mucosal injury and necrosis (cell death); these are not features of foreign body granulomatous inflammation.

Dr. Kane also inappropriately cites a number of studies in claiming that talc-induced inflammation causes specific biological responses that lead to ovarian cancer.[124] For example, Dr. Kane cites Buz'Zard 2007 in support of her claim that talc causes oxidative stress that can lead to the development of ovarian cancer.[125] But as Dr. Kane admitted, this study did not demonstrate increases in reactive oxygen species in ovarian cancer cells at 17 out of the 18 time points measured.[126] Moreover, this study is flawed in that it did not include negative controls, and it utilized immortalized ovarian surface epithelial and granulosa cell lines, which are not "normal." The only test of cell transformation used in the study was soft agarose growth and results of the talc studies were conflicting between the two cell lines used. In one cell line, a high dose suppressed soft agarose growth, but in the other cell line, it promoted soft agarose growth.

Similarly, Dr. Kane claims that Shukla 2009 demonstrates that "nonfibrous talc can induce an inflammatory response that alters expression of genes in cancer pathways" and "induces genotoxicity" in mesothelial cells.[127] Dr. Kane provides no analysis of the study to support these assertions, and the authors' statements directly contradict her characterization of the findings. Shukla et al. note that talc was used in this asbestos study as a nontoxic,

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122 Malmberg K, et al. Serous tubal intraepithelial carcinoma, chronic fallopian tube injury, and serous carcinoma development. *Virchows Arch*. 2016; 468(6):707-713.

123 Kane Report at 10.

124 Kane Report at 10-12.

125 Kane Report at 10.

126 Kane Deposition, pages 333-34.

127 Kane Report at 10, 36.

negative control that "is regarded as noncarcinogenic in humans."[128] The authors confirmed that, in contrast to asbestos, which "caused membrane blebbing and other toxic manifestations in cells," "particles of nonfibrous talc…were nontoxic."[129] Also contrary to Dr. Kane's suggestion that Shukla supports an inflammatory and pro-carcinogenic role for talc, talc had very little overall effect on gene expression in mesothelial cells compared to asbestos, and talc had no effect on ovarian cells. Among the few genes whose expression was increased by talc are those that have anti-inflammatory and anti-oxidant activities (ATF3 and SOD).

In addition, Dr. Kane cites a number of studies in support of her claim that talc induces macrophage TNF-alpha expression, which promotes ovarian carcinogenesis.[130] Of these, only the Hagemann study involved the ovaries, and that study cannot be used to support causation in humans because it used experimental ovarian cancer cell lines, which do not demonstrate the same molecular profiles as shown in tissue samples of ovarian cancer.[131] The Cheng, Yan and Xie studies were performed on rabbits, mice and rats, respectively, and did not evaluate ovarian cells or ovarian tissue. The Xie study also evaluated the effects of asbestos, not talc, on rat tracheal epithelium. The Nasreen and Van den Heuvel studies examined human mesothelial cells or patients undergoing pleurodesis; neither used ovarian tissue. In summary, apart from Hagemann, the studies cited by Dr. Kane not only failed to use ovarian tissue, but involve in vitro or animal models that are of questionable value in understanding ovarian carcinogenesis in humans.

Dr. Kane's claim that "there are experimental studies in the literature that support a causal relationship between talc and ovarian cancer," and that studies "show increases in inflammatory markers following talc exposure" is entirely false.[132] None of the studies Dr.

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[128] Shukla A, et al. Alterations in Gene Expression in Human Mesothelial Cells Correlate with Mineral Pathogenicity. *Am J Respir Cell Mol Biol.* 2009; 41:114-123.

[129] Shukla A, et al. (2009).

[130] Kane Report at 12 (citing Cheng DS, Rogers J, Wheeler A, et al. The effects of intrapleural polyclonal anti-tumor necrosis factor alpha (TNF alpha) Fab fragments on pleurodesis in rabbits. *Lung.* 2000;178(1):19–29; Hagemann T, Wilson J, et al. Ovarian cancer cells polarize macrophages toward a tumor-associated phenotype. *J Immunol.* 2006;176(8):5023–5032; Yan B, et al. Tumor necrosis factor-alpha is a potent endogenous mutagen that promotes cellular transformation. *Cancer Res.* 2006;66(24):11565–11570; Nasreen N, et al. Talc-induced expression of C-C and C-X-C chemokines and intercellular adhesion molecule-1 in mesothelial cells. *Am J Respir Crit Care Med.* 1998;158:971–978; van den Heuvel MM, et al. Talc-induced inflammation in the pleural cavity. *Eur Respir J.* 1998;12(6):1419–1423; Xie C, et al. TNF-alpha increases tracheal epithelial asbestos and fiberglass binding via a NF-kappaB-dependent mechanism. *Am J Physiol Lung Cell Mol Physiol.* 2000;279(3):L608–614).

[131] Domcke, et al. compared copy-number changes, mutations and mRNA expression profiles of 47 commonly used experimental ovarian cancer cell lines from the Cancer Cell Line Encyclopedia with ovarian cancer tumor samples from the Cancer Genome Atlas and found "pronounced differences in molecular profiles." Domcke S, et al. Evaluating cell lines as tumor models by comparison of genomic profiles. *Nature Commun.* 2013;4:2126. Accordingly, studies that utilize experimental ovarian cancer cell lines must be interpreted with caution, as these experimental cell lines do not reflect the molecular genetic characteristics of ovarian cancer tissues.

[132] Kane Report at 12 (citing Allaire GS, et al. Talc in liver tissue of intravenous drug abusers with chronic hepatitis. A comparative study. *Am J Clin Pathol.* 1989;92(5):583–588; Genofre EH, et al. Talc pleurodesis: evidence of systemic inflammatory response to small size talc particles. *Respir Med.* 2009;103(1):91–97; Arellano-Orden E, et al. Small particle-size talc is associated with poor outcome and increased inflammation in thoracoscopic pleurodesis. *Respiration.* 2013;86(3):201–209).

Kane cites has anything to do with ovarian cancer. Specifically, Allaire 1989 is a study of talc in liver tissue from IV drug users and Genofre 2009 and Arellano-Orden 2013 are studies of pleurodesis, which, as noted above, is a beneficial procedure that has not been reported to cause cancer and involves a part of the body that is unrelated to ovarian carcinogenesis.

In summary, Dr. Kane's theory that talc-induced inflammation causes ovarian cancer both fails to distinguish between specific types of inflammation and is not supported by the evidence she cites.

C. Detection of Talc in Ovarian Tissue

Dr. Kane's report includes a discussion of "talc in tissue."[133] Dr. Kane first describes certain microscopy and analytical techniques (polarized light microscopy, SEM and EDX) that she claims are used in surgical pathology. She then acknowledges that the presence of talc particles found in ovarian cancer tissue does not prove that the talc played a causal role, yet argues that it is "consistent with causation and provides additional evidence in support of a causal relationship."[134] This discussion is methodologically flawed for several reasons.

First, based on my experience as a surgical pathologist, ovarian cancer is never examined using the microscopy techniques Dr. Kane identifies. In fact, apart from the specific type of examination of breast tissues that Dr. Kane discusses, none of these techniques is used in general surgical pathology. Polarization is not routinely employed by surgical pathologists without some clear indication for doing so (e.g., confirmation of radiographic findings of breast calcifications or an observed foreign body reaction). Dr. Kane has admitted that polarized light microscopy is not routinely used to examine ovarian tumors.[135] Foreign body reactions and granulomas are easily detected by routine light microscopy.

Dr. Kane's reliance on Cramer 2007 is misplaced. Cramer 2007 is a case report of one patient, and therefore does not constitute meaningful scientific evidence supporting the allegation that talc causes ovarian cancer.[136] Indeed, the authors admit as much: "we are not claiming that a causal relationship between ovarian cancer and talc use is proven for this case or in general." They also acknowledge that "case reports cannot establish causality" and assert that "it is necessary to establish in a quantitative manner the likelihood of finding talc in lymph nodes of women with ovarian cancer and correlate this by whether they did or did not use talc." A similar study in ovarian tissue had already been done by Heller et al. in 1996, discussed below.

Second, as Dr. Kane concedes, the presence of talc particles in ovarian cancer tissue does not prove that the talc plays a causal role in the development of ovarian cancer. The development of the now well-established understanding that human papillomavirus (HPV) causes cervical cancer illustrates this principle. From the 1960s through the late 1980s, herpes

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133 Kane Report at 14-15.

134 Kane Report at 15.

135 Kane Deposition, page 108.

136 Cramer DW, et al. Presence of Talc in Pelvic Lymph Nodes of a Woman with Ovarian Cancer and Long-term Genital Exposure to Cosmetic Talc. *Obstet Gynecol*. 2007;110(2):498–501.

simplex virus (HSV) was thought to be the cause of cervical cancer. Electron microscopy revealed HSV particles in cervical cancer tissues,[137] and seroepidemiologic studies "confirming" that HSV was the causative agent showed that women with antibodies to HSV-2 were 10 times more likely to develop cervical cancer than women without antibodies to the virus.[138,139] Notably, the relative risks for HSV and cervical cancer reported in epidemiological studies far exceeded those that have been reported for talc and ovarian cancer. However, we now know that HPV, not HSV, causes cervical cancer; indeed, I have been involved with HPV vaccine clinical trials over the last 15 years and have seen a striking reduction in cervical cancer in countries where mandatory vaccination has been in place.[140] As this example illustrates, the fact that a particular agent has been observed in cancerous tissues, even combined with other apparently strong epidemiologic evidence, can lead to a flawed causal conclusion.

D. Migration of Talc to the Ovaries

Dr. Kane acknowledges that "for cosmetic talc applied to the perineum to reach the ovary or fallopian tube and exert a neoplastic effect, it needs to travel up through the vagina and uterus."[141] Without providing any analysis, Dr. Kane opines that: (1) it is "known" that "substances" can migrate through the genital tract to the ovaries; (2) studies have demonstrated talc in ovarian tissue; (3) a single case report of talc in pelvic lymph nodes supports inhalation and lymphatic transport as a "biologically plausible pathway"; and (4) the tubal origin of serous carcinoma is "not critical" to her opinions, because talc can migrate to both the fallopian tubes and ovaries. Elsewhere in her report, Dr. Kane opines that the protective effect associated with tubal ligation also supports her migration opinions.[142] Each of these claims lacks a scientifically valid basis.

First, Dr. Kane cites only two studies to support her opinion that migration through the genital tract to the ovaries is well established.[143] Neither of these studies replicated the type of exposure – external application to the vulva – reported by plaintiffs in this litigation, and neither study involved talc. Specifically, Venter 1979 introduced radioactive human albumin microspheres directly into the upper vagina of women undergoing elective gynecologic surgeries. Egli 1961 introduced carbon particles suspended in Dextran into the

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137 Aurelian L, et al. Herpesvirus type 2 isolated from cervical tumor cells grown in tissue culture. *Science*. 1971; 74:704-707.

138 Nahmias AJ and Roizman B. Infection with herpes-simplex viruses 1 and 2. *N Engl J Med*. 289(14):667,719-725.

139 Kaufman RH and Rawls WE. Herpes Genitalis and its Relationship to Cervical Cancer. *CA Cancer J Clin*, 1974; 24(5):258-265.

140 McGregor S, et al. Decline in prevalence of human papillomavirus infection following vaccination among Australian Indigenous women, a population at higher risk of cervical cancer: The VIP-I study. *Vaccine*. 2018;36(29):4311-4316.

141 Kane Report at 14.

142 Kane Report at 19.

143 Kane Report at 14 (citing Egli GE, Newton M. The transport of carbon particles in the human female reproductive tract. *Fertil Steril.* 1961;12:151–155; Venter PF, Iturralde M. Migration of a particulate radioactive tracer from the vagina to the peritoneal cavities and ovaries. *S Afr Med J.* 1979;55(23):917–919).

upper vagina of three anesthetized women undergoing elective hysterectomy, while simultaneously administering oxytocin to stimulate uterine contractions (hypothesized to facilitate transport to the ovaries). Notably, Dr. Kane omits any mention of Wehner 1985[144] and Boorman 1995.[145] Wehner examined talc migration in monkeys receiving repeated introductions of talc to the upper vagina over a period of 45 days. No talc particles were found in the uterus or tubes. Boorman analyzed ovaries from rats and mice exposed daily to aerosolized talc for two years. No talc particles were found in the animals' ovarian tissue, despite "ample opportunity for perineal as well as oral and respiratory exposure."[146] No ovarian tumors were found in exposed animals.

It should be noted that even when particles are placed into the vagina, passage to the ovaries is quite unusual. For example, in another study, it was reported that when India ink was introduced into the uterus, it was detected in the fallopian tubes in 50% of women and when introduced into the cervix, it was detected in the fallopian tubes of just 30% of women. When it was introduced into the vagina, it was detected in only one of 37 (0.02%) patients.[147] In short, the vulva is not an open conduit to the vagina and therefore none of these highly artificial studies can be used to assert that talc applied to the external perineum migrates to the fallopian tubes and ovaries. Finally, I note that Cramer 2007, which Dr. Kane relies on for her migration opinions, stated that "there is no proof that talc used externally reaches the pelvis."[148]

Second, the studies that Dr. Kane cites as finding talc in ovarian tissue do not support her contention that talc migrated there from the vulva through the reproductive tract.[149] The presence of talc in ovarian tissues can be easily explained as a contaminant. Talc is ubiquitous and is present in ceramic, paper, plastics, makeup, rubber and paint, all of which are present in pathology laboratories. Indeed, paper towels on which specimens are placed and cut to provide samples for microscopic analysis and lab counters are a very likely source of talc that can be introduced into tissues being processed for pathologic examination. Moreover, Heller, et al. attempted to correlate the observed talc content in benign ovaries with reported talc usage and found no difference between women who frequently applied talc and those who reported no use.[150] The results could be attributed to sample contamination, which is supported by the lack of any associated pathologic findings that

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144 Wehner AP et al. On talc translocation from the vagina to the oviducts and beyond. *Food Chem Toxicol,* 1986;24:329-338.

145 Boorman GA, Seely JC. A Lack of an Ovarian Effect of Lifetime Talc Exposure in F344/N Rats and B6C3F1 Mice. *Reg Toxicol Pharmacol*. 1995;2:242-243.

146 Boorman GA, Seely JC (1995).

147 De Boer CH. Transport of particulate matter through the human female genital tract. *J Reprod Fertil.* 1972;28(2):295-297.

148 Cramer DW, et al. (2007).

149 Kane Report at 14 (citing Henderson WJ, et al. Talc and carcinoma of the ovary and cervix. *J Obstet Gynaecol Br Commonw*. 1971;78(3):266–272; Henderson WJ, et al. Talc in normal and malignant ovarian tissue. *Lancet*. 1979;313(8114):499; Mostafa SA, et al. Foreign body granulomas in normal ovaries. *Obstet Gynecol.* 1985;66(5):701–702; 22; Heller DS, et al. The relationship between perineal cosmetic talc usage and ovarian talc particle burden. *Am. J. Obstet. Gynecol*. 1996;174(5):1507–1510).

150 Heller DS, et al. (1996).

would indicate actual biologic exposure. In fact, Heller noted that hematoxylin-eosin (H&E) examination of high-burden ovaries did not reveal any associated granulomas or foreign body giant cells.

Third, Dr. Kane's opinion that inhalation and lymphatic transport is "another biological pathway"[151] is speculative and not supported by evidence demonstrating that inhaled talc can reach the ovaries through the lymphatic system. If inhalation of talc were a significant route of exposure to ovarian tissue, one would expect to see evidence of talc-induced pulmonary diseases in women who use perineal talc. I am not aware of any such reports. The studies Dr. Kane relies on to support inhalation exposure to ovarian tissue are inapplicable: Cramer 2007 is only a case report of a single patient and provides no data to support inhalation as a route of exposure; Suzuki involved inhaled asbestos fibers in occupationally exposed men; Marchiori involved pulmonary complications of inhaled or injected talc; and Frank involved pulmonary talcosis as a result of inhaled talc.

Fourth, Dr. Kane is correct that there is evidence that "serous ovarian cancers are actually of fallopian tube origin," but Dr. Kane's opinion that this information is "not critical" to the question at hand is clearly wrong.[152] To the contrary, it is extremely important and significantly undermines the theory that talc use causes serous ovarian cancer, since cancer biologists agree that an understanding of carcinogenesis of a tumor begins with determining the genetic alterations that occur in the tissue (organ) of origin – not in the organs to which the primary tumor has spread. The evidence that serous ovarian cancer originates in the fallopian tubes invalidates many of Dr. Kane's more specific opinions, since the biologic evidence she presents often relates to events occurring on the ovarian surface epithelium, implying that ovarian cancer originates there, rather than in the fallopian tubes.[153] In fact, Dr. Kane does not cite any studies to support her biological plausibility opinions that involve the fallopian tube epithelium.

Relatedly, the fallopian tube origin of serous carcinoma also undermines Dr. Kane's argument that tubal ligation and hysterectomy decrease the risk of "talc-associated ovarian cancer" "by impeding the proximal migration of talc into the perineum to the ovaries and fallopian tubes."[154] Disruption of particle migration has been hypothesized to explain the observed reduction in risk of ovarian cancer associated with these procedures in the epidemiologic literature. However, there is strong evidence that these procedures are protective against ovarian cancer for reasons unrelated to this hypothesis. Specifically, hysterectomy and tubal ligation prevent retrograde menstruation, which is regarded as one of the major mechanisms for the development of endometriosis, thereby reducing the risk of

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[151] Kane Report at 14 (citing Suzuki Y, Kohyama N. Translocation of inhaled asbestos fibers from the lung to other tissues. *Am J Ind Med*. 1991;19(6):701–704; Marchiori E, et al. Pulmonary talcosis: imaging findings. *Lung*. 2010;188(2):165–171; Frank C LJ. An uncommon hazard: pulmonary talcosis as a result of recurrent aspiration of baby powder. *Respiratory Med CME*. 2011;4(3):109–111).

[152] Kane Report at 14.

[153] *E.g.*, Kane Report at 12 (citing Richards JS, et al. Ovulation: New dimensions and new regulators of the inflammatory-like response. *Annu Rev Physiol*. 2002;64:69–92 for the premise that ovulation causes an "inflammatory response to disruption of the ovarian epithelium").

[154] Kane Report at 19, 36 (citing Green A, Purdie D, Bain C, et al. Tubal sterilization, hysterectomy and decreased risk of ovarian cancer. Survey of Women's Health Study Group. *Int J Cancer*. 1997;71:948–951.).

endometrioid and clear cell carcinoma.[155] It has also been demonstrated in humans and mouse models that tubal ligation is associated with "a reduced presence and decreased proliferation of progenitor cells in the distal fallopian tube epithelium," "compositional and functional changes [that] suggest that tubal ligation induces quiescence of distal fallopian tube epithelial cells."[156] This explains the reduction in risk of HGSC, which, as explained above, arises from the fallopian tube epithelium (and mainly at the distal end of the fallopian tube). Accordingly, these mechanisms alone reduce the risk of developing ovarian cancer without having to implicate the particle migration hypothesis Dr. Kane endorses.[157]

CONCLUSION

Based on my extensive experience studying ovarian cancer pathology, I find that Dr. Kane's opinion that talc use causes ovarian cancer is not scientifically justified. Moreover, Dr. Kane's opinions are inconsistent with the consensus view of the scientific community regarding what is currently known about ovarian cancer pathology.

First, ovarian cancer is a diverse group of neoplasms (high-grade serous, low-grade serous, endometrioid, clear cell, seromucinous, and mucinous carcinomas and malignant Brenner tumors) with different morphology, pathogenesis, molecular genetic features and behavior that are distinct from mesothelioma. It is highly unlikely that one agent, i.e., talc, is a cause of these different tumors, and there are no studies linking talc exposure to the specific genetic alterations associated with the development of these tumors. Second, carcinomas arise from molecular genetic alterations in specific organ sites. Mesothelium, the site of origin of mesotheliomas, is distinct in morphology and molecular genetic features from tubal epithelium and endometrial tissue, the respective sites of origin of HGSC and endometrioid and clear cell carcinomas. Third, the studies that are cited to support chronic inflammation as a cause of cancer are not relevant to talc-associated inflammation, because the type of inflammation cited is not the type of foreign body granulomatous inflammation associated with talc exposure. Fourth, observations of talc in ovarian tissue do not support a conclusion of causation. Fifth, there are no animal or histologic data supporting the genital migration of talc applied externally to the vulva. Finally, talc has been used for many years as a treatment ("pleurodesis") for benign recurrent pneumothorax and pleural effusions, which severely restrict the patient's ability to breathe. Talc pleurodesis involves the installation of large amounts of talc directly into the pleural space to cause a marked foreign body granulomatous response and fibrosis that compress the pleural cavity, alleviating the difficulty in breathing. If talc exposure caused cancer, one would expect that some of the patients treated for benign conditions would develop cancer in the future. Long-term studies have not demonstrated this to be the case.

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155 Rosenblatt KA, et al. (1996).

156 Tiourin E, et al. (2015).

157 Of note, Green 1997 showed only a slightly increased risk of ovarian cancer (RR 1.3, CI 1.1-1.6) among women with patent fallopian tubes who used talc in the perineal region compared to women who did not use talc. The study also described that women who reported heavy or painful menses were also found to have a higher risk of ovarian cancer, and that reduction in risk of disease after hysterectomy was greatest among women who had heavy periods. This suggests that retrograde menstruation or endometriosis may have been a confounding variable in this study, reminiscent of HSV and cervical cancer, as discussed above.

APPENDIX 1

The following provides additional detail regarding the molecular genetic features of the various subtypes of non-high-grade serous epithelial ovarian cancer. Most of this information can be found in Kurman RJ, Shih I-M (2016) and has been adapted for brevity and convenience here.

Molecular genetic features of low-grade serous carcinoma

The MAPK pathway plays a critical role in the transmission of growth signals into the nucleus and ultimately contributes to neoplastic transformation. *KRAS* mutations at codons 12 and 13 occur in one-third of APSTs and LGSCs, and *BRAF* mutations at codon 600 occur in another one-third of APSTs, but less commonly in LGSCs.[158] Mutations of *ERBB2* occur in less than 5% of these tumors; *NRAS* mutations are also detected in a small percentage of LGSCs.[159] Mutations in *KRAS, BRAF* and *ERBB2* are mutually exclusive and consequently are detected in about two-thirds of APSTs and LGSCs. They appear to occur early in the development of these tumors, as evidenced by the finding of *KRAS* and *BRAF* mutations in the benign cystadenoma epithelium adjacent to APSTs.[160] Pure serous cystadenomas do not harbor these mutations, supporting the interpretation that these mutations are critical in initiating the LGSC pathway. It has been speculated that *BRAF* and *KRAS* mutations are responsible for tumor initiation, which results in oxidative stress leading to DNA double strand breaks. *BRAF* mutation in particular activates the p53/p16/p21 pathway, leading to arrest of cell growth. Most of these tumors do not progress to LGSC, but some do. Progression from an APST to LGSC appears to result when additional molecular alterations abolish the checkpoint control. (For example, deletion of ch1p36, which contains a region with several candidate tumor suppressor genes that regulate cellular proliferation and apoptosis, may abolish the p53 checkpoint permitting tumor cells to proliferate and become aggressive.)

Molecular genetic features of endometrioid carcinoma

Inactivating mutations of *PTEN* and activating mutations of *PIK3CA* can lead to activation of the PI3K signaling pathway, which has been implicated in malignant transformation. Less than 7% of endometrioid carcinomas have activating mutations in *KRAS* and *BRAF*.[161] Microsatellite instability has also been reported in up to 20% of endometrioid carcinomas, and is usually associated with loss of hMLH1, hMSH2, MSH6 and PSM2 expression. Mutation of the tumor suppressor gene, *ARID1A*, occurs in approximately 30% of

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158 Kurman RJ, Shih I-M. (2016) (citing Singer G, et al. (2003); Jones S, et al. Low-grade serous carcinomas of the ovary contain very few point mutations. *J Pathol.* 2012, 226(3):413-420).

159 Kurman RJ, Shih I-M. (2016) (citing Jones S, et al. (2012); Emmanuel C, et al. Australian Ovarian Cancer Study (AOCS): Genomic classification of serous ovarian cancer with adjacent borderline differentiates RAS pathway and TP53-mutant tumors and identifies NRAS as an oncogenic driver. *Clin Cancer Res.* 2014, 20(24):6618-6630).

160 Kurman RJ, Shih I-M. (2016) (citing Ho, CL, et al. Mutations of BRAF and KRAS precede the development of ovarian serous borderline tumors. *Cancer Res.* 2004, 64(19):6915-6918).

161 Kurman RJ, Shih I-M. (2016) (citing Wu R, et al. (2007); Mayr D, et al. KRAS and BRAF mutations in ovarian tumors: A comprehensive study of invasive carcinomas, borderline tumors and extraovarian implants. *Gyn. Oncol.* 2006; 103(3):883-887).

endometrioid carcinomas. Notably, endometrioid carcinoma of the ovary, unlike high-grade serous carcinoma, is not associated with germline mutations of *BRCA1/2* but may be associated with Lynch syndrome, an inherited condition that also increases the risk of colorectal and uterine carcinoma and less frequently other malignancies.

Molecular genetic features of clear cell carcinoma

Inactivating mutations of *PTEN* and activating mutations of *PIK3CA* can lead to activation of the phosphatidylinositol 3- kinase signaling pathway. The similar molecular genetic profiles of endometrioid and clear cell carcinomas highlight their close relation and origin from endometriosis. However, the morphology and behavior of endometrioid and clear cell carcinomas are different, so it is not surprising that, e.g., canonical Wnt signaling pathway defects and microsatellite instability have not been observed with significant frequency in clear cell tumors, unlike endometrioid tumors.[162] Studies that used genetically engineered mouse models found that deletion of *ARID1A*, mimicking its somatic inactivation, is insufficient to drive ovarian tumor formation; however, codeletion of *ARID1A* and *PTEN* results in ovarian endometrioid carcinoma,[163] whereas codeletion of *ARID1A* and *PIK3CA* leads to formation of clear cell-like ovarian neoplasms in mice.[164] In addition to these molecular genetic alterations, a recent genome-wide methylation study suggested that clear cell carcinomas have a unique methylation profile compared with the other histologic subtypes.[165] Pathway analyses indicate that there is an increase in promoter methylation for multiple genes in the ER pathway and loss of promoter methylation for multiple genes in the hepatocyte nuclear factor 1 (HNF1) pathway, thus explaining the characteristic immunohistochemical findings in clear cell carcinomas. *TP53* mutations were described in high-grade endometrioid carcinoma with expression profiles similar to those of HGSC, but these tumors may have been misclassified, as suggested by more recent studies reporting a subset of HGSCs that display a pseudoendometrioid pattern.[166]

Molecular genetic features of mucinous carcinoma

Interestingly, mutations in *KRAS*, *BRAF* and/or *ERRB2* amplification are present in >90% of mucinous carcinomas, indicating frequent RAS/MEK pathway activation in this neoplasm. Another study identified mutations in a novel gene, *RNF43*.[167] By combining the

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[162] Kurman RJ, Shih I-M. (2016) (citing Willner J, et al. Alternate molecular genetic pathways in ovarian carcinomas of common histological types. *Hum Pathol.* 2007, 38(4): 607-613).

[163] Kurman RJ, Shih I-M. (2016) (citing Guan B, et al. Roles of deletion of Arid1a, a tumor suppressor, in mouse ovarian tumorigenesis. *J Nat'l Cancer Inst.* 2014;106(7)).

[164] Kurman RJ, Shih I-M. (2016) (citing Chandler RL, et al. Coexistent ARID1-APIK3CA mutations promote ovarian clear-cell tumorigenesis through pro-tumorigenic inflammatory cytokine signalling. *Nat Commun.* 2015;6:6118).

[165] Kurman RJ, Shih I-M. (2016) (citing Yamaguchi K, et al. Epigenetic determinants of ovarian clear cell carcinoma biology. *Int J Cancer.* 2014, 135(3): 585-597).

[166] Kurman RJ, Shih I-M. (2016) (citing Soslow RA, et al. (2012)).

[167] Kurman RJ, Shih I-M. (2016) (citing Ryland GL, et al. RNF43 is a tumour suppressor gene mutated in mucinous tumours of the ovary. *J Pathol.* 2013;229:469-476).

discovery and validation sets, 6 of 29 mucinous carcinomas (21%) were found to harbor the inactivating mutations of *RNF43*, a zinc finger-dependent E3 ubiquitin protein ligase, suggesting that *RNF43* inactivation may characterize a proportion of mucinous cancers.[168]

Molecular genetic features of malignant Brenner tumor

There have only been a few immunohistochemical and molecular genetic studies of benign and atypical proliferative Brenner tumors. p16 immunostaining was shown to be positive in the epithelial component of 12 of 13 benign Brenner tumors (92%) but completely negative in 7 atypical proliferative Brenner tumors. Fluorescence in situ hybridization identified homozygous deletion of *CDKN2A*, the gene encoding p16, in the epithelial component of all atypical proliferative tumors, but it was retained in all benign tumors. Two *PIK3CA* mutations were found in the stromal component in 2 of 20 benign Brenner tumors (5%) but not in the epithelial component. However, one *KRAS* mutation and two *PIK3CA* mutations were detected in the epithelial component of two atypical proliferative tumors (29%).[169] These findings suggest that loss of *CDKN2A* may play a role in progression of benign to atypical proliferative Brenner tumors.

[168] Kurman RJ, Shih I-M. (2016) (citing Ryland GL, et al. (2013)).

[169] Kurman RJ, Shih I-M. (2016) (citing Kuhn E, et al. Molecular characterization of undifferentiated carcinoma associated with endometrioid carcinoma. *Am J Surg Pathol*. 2014, 38(5):660-665).

APPENDIX 2

Glossary of Selected Pathology Terms

Ascites: Fluid in the abdomen. This can be malignant when associated with a carcinoma. It is often present in ovarian cancer. It can also be benign, particularly when it is associated with liver disease, such as cirrhosis.

Atypia: The degree to which the nuclei in the cells of a tumor differ from the normal appearance. The higher the grade, the more aggressive the tumor is. Usually expressed as well, moderately or poorly differentiated. Alternatively, a numbering system is used. Grade 1,2,3.

Clone: One or a group of genetically identical cells

Foreign body giant cell: A multinuclear cell resulting from the fusion of macrophages that is elicited in response to a foreign body, such as a suture or, in the case of this litigation, talc.

Germline mutation: A mutation occurring in the cells of the zygote (fertilized ovum) and therefore occurring in all the cells of the body. As these mutations are present in oocytes and sperm, they can be passed on to the progeny.

Granuloma: A nodular aggregation of mononuclear inflammatory cells, generally macrophages reassembling epithelial cells (epithelioid cells), usually surrounded by a rim of lymphocytes, often with multinucleated giant cells.

Hyperplasia: Cellular growth that is beyond what is normally seen in a particular tissue. The significance of this feature is that besides growing more rapidly, highly proliferating cells have a greater chance of undergoing a mutation leading to malignant behavior.

Ovarian Cancer: There are five major subtypes: epithelial, germ cell, gonadal stromal, nonspecific and metastatic.

Epithelial ovarian carcinomas:

Serous [low-grade and high-grade] – These tumors bear a resemblance to fallopian tube epithelium and are derived from the fallopian tube.

Endometrioid – These tumors bear a resemblance to the endometrium (lining of the uterine cavity) and arise from endometriosis or an endometriotic cyst.

Clear cell – These tumors are related to endometrioid carcinoma, but the cells contain clear cytoplasm and also arise from endometriosis.

Seromucinous – These tumors are composed of a variety of different cell types including serous, mucinous and endometrioid cells. They are also derived from endometriosis.

Mucinous – These tumors contain abundant mucin in the cytoplasm and superficially resemble tumors from the gastrointestinal tract.

Malignant Brenner tumor – These tumors are composed of transitional epithelium

resembling the tissue that lines the urinary bladder.

Carcinosarcoma – A highly malignant tumor that has the appearance of both a carcinoma and a sarcoma. Recent immunohistochemical and molecular genetic studies indicate that these are essentially carcinomas that have a component that simulates a sarcoma.

Germ cell tumors: Several different tumor types derived from the primitive germ cells of the embryonic gonad. The different types are listed below, but are not described in detail because they are not the subject of this litigation.

Dysgerminoma

Embryonal carcinoma

Yolk sac tumor

Choriocarcinoma

Teratomas

Sex cord stromal tumors: Several tumor types derived from the stomal component of the ovary, which is responsible for the production of steroid hormones. Accordingly, several of these tumors may secrete estrogens or androgens. The different types are listed below, but are not described in detail because they are not the subject of this litigation.

Granulosa tumors

Thecoma

Sclerosing stromal tumor

Microcystic stromal tumor

Signet stroma tumor

Sertoli Leydig tumor

Stromal luteoma

Nonspecific tumors: There are 30 different tumor types in this category. As with the germ cell and sex cord stromal tumors, they are not described in detail because they are not the subject of this litigation.

Metastatic tumors: Many tumors from other sites of the body can spread to the ovary, but for all practical purposes only about 20 are the most common, such as tumors from the gastrointestinal tract and breast. As with the germ cell and sex cord stromal tumors, they are not described in detail because they are not the subject of this litigation.

Neutrophils, lymphocytes, plasma cells, histiocytes (macrophages): These are mononuclear cells involved in the immune response, both cellular and humoral (production of antibodies,

particularly by plasma cells).

Omentum: A fold of peritoneum, composed mostly of fat, extending, like an apron, from the stomach to adjacent organs in the abdominal cavity.

Papillary: A growth pattern characterized by finger-like extensions from the tumor mass. This descriptive term can be applied to either the gross or microscopic features of a tumor.

Somatic mutation: Mutations occurring in different cells in the body. These occur after birth; in other words, the individual was not born with these mutations, in contrast to germline mutations.

Stage: The extent to which a tumor has spread at the time of diagnosis. This is determined both by the findings at surgery and by the microscopic findings (pathologic diagnosis).

Tumor grade: This describes the aggressiveness of a tumor based on certain microscopic features, mainly nuclear (also referred to as cytologic) atypia.

EXHIBIT A

Curriculum Vitae

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Revised: 2/22/2019

Date of Birth:

November 20, 1943

College:

Queens College, B.A., New York, 1964

Medical School:

Upstate Medical Center,
Syracuse, New York, 1968

Internship:

Medicine and Pathology, Beth Israel Hospital, New York, 1969

Residency and Training:

Pathology, Peter Bent Brigham Hospital, Boston, 1969-70
Pathology, Children's Hospital and Boston Hospital for Women, Boston, 1970-71
Pathology, Massachusetts General Hospital, Boston, 1971-72
Obstetrics & Gynecology, Boston Hospital for Women, Boston, 1972-73
Obstetrics and Gynecology, Los Angeles County Hospital/University of Southern California, Los Angeles, 1976-78

Academic and Hospital Appointments:

Clinical Fellow in Obstetrics and Gynecology, Harvard Medical School, Boston, 1972
Assistant Chief, Department of Gynecology and Breast
Pathology, Armed Forces Institute of Pathology, Washington, D.C., 1973-76
Assistant Professor, Pathology, University of Southern California, Los Angeles, 1976-78
Associate Professor, Pathology and Obstetrics and Gynecology, Georgetown University School of Medicine, Washington, D.C., 1978-82
Associate Professor, with tenure, Pathology and Obstetrics and Gynecology, Georgetown University School of Medicine, 1983-86
Professor, Pathology and Obstetrics and Gynecology, Georgetown University School of Medicine, 1986-88
Richard W. TeLinde Professor of Gynecologic Pathology, Departments of Gynecology-Obstetrics and Pathology, The Johns Hopkins University School of Medicine, 1989

Director of Gynecologic Pathology, The Johns Hopkins Hospital, 1989
Richard W. TeLinde Distinguished Professor of Gynecologic Pathology, 1998
Professor of Oncology, The Johns Hopkins University School of Medicine, 2003

Awards:

Phi Beta Kappa, 1964
Presidential Award for Best Scientific Presentation, Society of Gynecologic Oncology, 1985
Recognition Award, International Academy of Pathology, 1987
Presidential Award for the Best Paper, Society of Gynecology Oncology, 1988
National Faculty Award for Excellence in Resident Education in Obstetrics and Gynecology, 1994
Alpha Omega Alpha, 2004
The Fred W. Stewart Award of Memorial Sloan Kettering Cancer Center, 2009
Maude Abbott Lecturer, USCAP meeting, Vancouver, 2012
Honorary Fellow, Royal College of Pathologists, 2013
Distinguished Alumnus Award, Upstate Medical Center, State University of New York at Syracuse, 2013
Honorary Member, Austrian Society of Pathologists, 2014

Consultant:

Visiting Scientist – Armed Forces Institute of Pathology, 1982-1993, Review Panel Pathologist, Cancer and Steroid Hormone (CASH)CDC-NIH Grant, 1982-84
Consultant – Coordinating Pathologist – Westat – NCI
Contract – Epidemiologic Study of Black/White Differences in Cancer Patient Survival Experience, 1983-87
Integration Panel Member – Department of Defense Congressionally Directed Medical Research Program in Ovarian Cancer, 1997-00
Consultant – American Registry of Pathology, 1998
Consultant – Armed Forces Institute of Pathology, 2002

Scientific Advisory and Editorial Boards:

Editorial Board, International Journal of Gynecological Pathology, 1982
Editorial Board, Seminars in Diagnostic Pathology, 1983
Editorial Board, Modern Pathology, 1987-2005
Editorial Board, Surgical Pathology, 1988
Editorial Board, Journal of Gynecologic Surgery, 1989
Scientific Advisory Board, American Registry of Pathology, 1991
Editorial Board, Gynecologic Oncology, 1992
Editorial Board, Cancer Cytopathology, 1996
Editorial Board, International Journal of Surgical Pathology, 1993
Editorial Board, Human Pathology, 1999
Editorial Advisory Board, American Journal of Obstetrics and Gynecology, 2006
Scientific and Medical Advisory Board, Ovarian Cancer National Alliance, 2009

Reviewer:

Cancer
American Journal of Surgical Pathology
Obstetrics and Gynecology
Journal of Histochemistry and Cytochemistry

Journal of the National Cancer Institute
Archives of Pathology and Laboratory Medicine
Laboratory Investigation
Journal of the American Medical Association
American Journal of Obstetrics and Gynecology
Placenta
American Journal of Pathology
New England Journal of Medicine
Human Pathology
Proceedings of the National Academy of Sciences, USA
International Journal of Cancer

Diplomate and Fellow:

National Board of Medical Examiners, 1969
American Board of Pathology, 1972
American Board of Obstetrics and Gynecology, 1980
American College of Obstetrics and Gynecologists, 1981

Professional Societies:

Washington, D.C., Society of Pathologists, 1974 (President 1986-87)
International Academy of Pathology, 1975
American Society of Clinical Pathologists, 1975
International Society of Gynecologic Pathologists, 1978
- Secretary 1998-2003
- Vice President 2004-05
- President 2006-2008

Medical Society of the District of Columbia, 1979
Society of Gynecologic Oncologists, 1979
Arthur Purdy Stout Society of Surgical Pathologists, 1980
American Medical Association, 1980
New York Academy of Science, 1982
International Gynecologic Cancer Society, 1985
- Executive Council, Pathology Representative, 2008
- Senior Member. 2016

Western Society of Gynecologic Oncology (Honorary Member), 1986
American Society for Colposcopy and Cervical Pathology, Board of Directors, 1990
The Howard A. Kelly Gynecologic and Obstetric Society (Founding member), 1991

Licensure:

New York, #105345, 1969
Washington, D.C., #6781, 1973
Maryland, #D17627, 1975
California, #G35167, 1977
Nevada, #12727, 2008

National Committees:

Member, Pathology Committee, Gynecologic Oncology Group, 1978
Member, Endometrial Cancer Committee, Gynecologic Oncology Group, 1979
Member, Membership Committee, Gynecologic Oncology Group, 1980

Member, Cancer Task Force, American Society of Clinical Pathologists, 1981
Member, Program Committee, Society of Gynecologic Oncology, 1982, 1988
Member, Endometrial Cancer Nomenclature Committee, International Society of Gynecological Pathologists and WHO, 1983
Chairman, Trophoblastic Disease Nomenclature Committee, International Society of Gynecological Pathologists and WHO, 1983
Member, Executive Committee, Gynecologic Oncology Group, 1984
Member, Cervical Cancer Nomenclature Committee, International Society of Gynecological Pathologists, 1987
Member, Task Force on Hysterectomy, American College of Obstetrics and Gynecology, 1988
Member, Committee on Human Research, American College of Obstetrics and Gynecology, 1988-89
Member, Prolog Task Force, American College of Obstetrics and Gynecology, 1988-1990
Member, Working Group, The Bethesda System for classification of cervical and vaginal cytology, 1988
Chairman, The Second Bethesda System Conference, National Cancer Institute, Bethesda, 1991
Member, Editorial Committee, The Second Bethesda System, 1991
Chairman, Criteria Committee, The Second Bethesda System, 1991
Chairman, Committee for Development of Provisional Guidelines for the Management of Abnormal Pap Smears, NCI, Bethesda, 1992
Member, Detection & Treatment Advisory Group on Gynecological Cancer, American Cancer Society, 1993
Member, American Cancer Society Task Force on Gynecologic Cancer, 1993
Member, Detection & Treatment Advisory Group on Gynecological Cancer, American Cancer Society, 1994
Member, Prolog Task Force, American College of Obstetrics & Gynecology, 1994-1995
Member, Congressionally Directed Medical Research Program, Ovarian Cancer Integration Panel, 1997-present
Member, Nomenclature Committee, International Society for the Study of Gestational Trophoblastic Disease, 1999
Member, American Joint Committee on Cancer's Gynecologic Task Force, 2000
Member, Scientific and Medical Advisory Committee of the Ovarian Cancer and National Alliance, 2006
Member, International Federation of Gynecology and Obstetrics (FICO) Committee, 2006
Chairman Nomenclature Committee, International Society of Gynecological Pathologists, 2011

Hospital and Medical School Committees:

Executive Faculty Committee, Department of Gynecology and Obstetrics, 1989 - to present
Executive Faculty Committee, Department of Pathology, 1989-1993

Visiting Professorships and Endowed Lectures:

University of Virginia, Charlottesville – Thornton Symposium, Keynote Speaker - The 6th Annual John M. Nokes Lecture, 1984
University of Connecticut Health Center, Feature Speaker at Third Annual Ella T. Grasso Memorial Conference, 1984
Booth Memorial Hospital First Ancel Blaustein Memorial Lecture, New York, 1985
University of Rochester Medical Center, The Eighth Annual Dr. Jerome H. Rudolph Memorial Lecture, 1989
University of California, Irvine, The Shirley Nissen Lecture, 1989
Baptist Memorial Hospital, The Merlin L. Trumbull Lectureship in Pathology, Memphis, 1989
Brigham and Womens Hospital, 75th Anniversary Celebration, Distinguished Alumni Pathology Symposium, 1989
St. Johns Mercy Medical Center, The Fredrick Germuth Memorial Lecture, St. Louis, 1990
Jefferson Medical College, The Warren Lang Memorial Lecture, Philadelphia, 1990
University of Pittsburgh, Magee-Womens Hospital, The Second Annual Aron E. Szulman Lecture, Pittsburgh, Pennsylvania, 1990
University of Western Ontario, School of Medicine, The Paterson Memorial Lecture, London, Ontario, 1990
George Washington University, School of Medicine, The Alexander Breslow Memorial Lecture, Washington, D.C., 1991
University of Michigan, School of Medicine, The First John R.G. Gosling Lecture, Ann Arbor, 1991
University of Minnesota, School of Medicine, Robert O. Meyer, Lectureship in Gynecologic Pathology, 1991
Albert Einstein College of Medicine, The Fifth Annual Herbert G. Winston Lecture in Obstetrics and Gynecology of the Raymond and Beverly Sackler Foundation, New York, 1991
Pennsylvania Hospital, The Nineteenth Annual S. Leon Israel Memorial Lecture, Philadelphia, 1991
University of South Florida, Tampa, 1991
California Pacific Medical Center, San Francisco, Koret Visiting Professor, 1992
Tulane University School of Medicine, The Fifth William Sternberg Memorial Lecture, New Orleans, 1994
Emory University, Atlanta, Georgia, 1996
Stanford University, Stanford, California, 1996
Kaiser Permanente Hospital, San Francisco, California, 1996
The James Platt-White Memorial Lecture, Buffalo Gynecologic and Obstetric Society, Buffalo, New York, 1996
The University of Iowa, Iowa City, Iowa, 1996
The First Pasman Visiting Professor, Vrije Universiteit, Amsterdam, 1996
University of Graz, Graz, Austria, 1996
University of Vienna, Vienna, Austria, 1998
University of Tel-Aviv, Tel-Aviv, Israel, 1998
The John B. Holyoke Surgical Pathology Lecture, Denver, Colorado, 1998
Wilford Hall Airforce Hospital, San Antonio, Texas, 1999
Rush-Presbyterian – St. Luke's Medical Center, Chicago, Illinois, 2000

1st Dinh-Doherty-Hannigan Lecture in Gynecologic Pathology, Galveston, Texas, 2000
Alexander P. Papamarkou Lecture, Memorial Sloan-Ketting Cancer Center, NY, NY, 2001
Penrose Hospital, Colorado Springs, Colorado, 2001
Madigan Army Medical Center, Takoma, Washington, 2001
Armed Forces Institute of Pathology, Washington DC, 2002
Jefferson Medical College, The 14th Annual Warren Lang Memorial Lecture, 2002
The Seventh Annual Mathews Distinguished Visiting Professor of Pathology at Emory University, Atlanta, Georgia, 2002
University of Bologna, Department of Obstetrics and Gynecology, 2004
University of Rome, Department of Pathology, 2004
University of Michigan, Department of Pathology, 2004
University of Basel, 150th Anniversary of the Pathology Institute, Basel, Switzerland, 2005
Yale University School of Medicine, Department of Obstetrics and Gynecology, 2008
Warren Lang Lectureship, Jefferson University School of Medicine, 2008
Lauren Ackerman Memorial Lectureship, Washington University, St. Louis, 2008
Beth Israel and Deaconess Hospital, Harvard Medical School, Boston, Mass, 2009
Rush Presbyterian Medical Center, Chicago, Illinois, 2009
Marmara University, Istanbul, Turkey, 2009
Annual Dr. Marie-Claire Marroum lecture, Charlotte, North Carolina, 2010
University of Iowa, 2010
Distinguished Lecturer, Fox Chase Cancer Center, Philadelphia, PA, 2011
Key Note Speaker, 13th National Gyncecological Oncology Congress, Turkish Society of Gynecological Oncology, Antalya, Turkey, 2012
Key Note Speaker, 22nd Annual Meeitng of the Japanese Society of Gynecological Cancer Screening, Kumamoto, Japan, 2013
Visiting Ptofessor, First Annual Christl Burgess Memorial Lecture, Loyola University Medical Center, Chicago, 2014
Visiting Professor University of Florida College of Medicine, Gainesville, 2014
Keynote Speaker The 32 Annual Resident Research Symposium, Department of Pathology, University of Florida, Gainesville, 2014
Visiting Professor Montefiore Hospital and Albert Einstein Medical School, Bronx, New York, 2014
Visiting Professor Stanford University. The First Michael R. Hendrickson, MD Lecturship in Surgical Pathology, Palo Alto, CA, 2015
Visiting Professor Cleveland Clinic. Cleveland, 2015
2015 Eleanor Humphreys Visiting Professor in Surgical Pathology, University of Chicago, 2015
Visiting Professor, Emory University School of Medicine Atlanta, 2015
Visiting Professor, McGill University, School of Medicine, Finlayson Lecture, Montreal, 2016

Visiting Faculty – Postgraduate Courses:

Member, Gynecologic Pathology Course, Armed Forces Institute of Pathology, 1973-1994
Director, Workshop on Endocrine Pathology of the Female Genital Tract, American Society of Clinical Pathology, 1975-79
Member, Workshop on Diagnostic Problems in Gynecologic Pathology, American Society of Clinical Pathologists, 1976-77
Member, Gynecologic Pathology Specialty Conference, International Academy of Pathology, 1977
Member, Postgraduate Course in Obstetrics and Gynecology, University of Southern California,

Los Angeles, 1978
Member, Gynecologic and Obstetrics Pathology Course, Harvard Medical School, Boston, 1979-1990
Member, Preinvasive and Early Invasive Tumors of the Female Genitalia, University of Tennessee, Center for Health Sciences, Memphis, 1979
Moderator, Symposium on Recent Advances in Gynecologic Pathology, Joint Meeting, Washington, D.C. and Maryland Society of Pathologists, Bethesda, 1979
Member, Testicular Tumor Pathology Panel, Minneapolis, 1980
Member, Gynecologic Pathology Course, American College of Obstetricians and Gynecologists, Armed Forces District Meeting, Phoenix, 1981
Member, Gynecologic Oncology Course, Georgetown University School of Medicine, 1981-85
Director, Pathology of the Ovary, Short Course, Inter national Academy of Pathology, 1981-86
Member, J. Donald Woodruff Symposium on Gynecologic Oncology, Baltimore, 1982, 1983, 1988, 1989, 1990, 1991
Member, Obstetric and Gynecologic Pathology Course, American College of Obstetrics and Gynecology, 1982-86
Director, Advances in the Application of Immunocytochemistry in Surgical Pathology, Specialty Course, International Academy of Pathology, 1983, 1985, 1987
Moderator, Scientific Session, Society of Gynecologic Oncology Meeting, Scottsdale, 1983
Member, Problems in Surgical Pathology, National Institutes of Health, 1983-1991
Member, Selected Topics in Surgical Pathology, Short Course, American Society of Clinical Pathology, 1984-87
Member, Gynecologic and Obstetrics Pathology Course with Clinical Correlation, University of Alicante, Spain, 1984
Member, Controversies in Surgical Pathology, American Society of Clinical Pathology, New Orleans, 1984
Member, Laser Surgery in Gynecology and Hysteroscopy, Columbia Hospital for Women, Wash., D.C., 1984-1991
Member, Surgical Pathology Review Course, University of Texas, Dallas, 1985
Member, Johns Hopkins Review Course in Reproductive Endocrinology, General Gynecology, and Gynecologic Oncology, Hilton Head, 1985, 1989
Member, Update in Gynecologic Oncology, St. John's Hospital, Detroit, 1985
Member, International Society of Gyneoclogical Pathologists' Symposium on Immunocytochemistry in Gynecological Pathology, Sendai, Japan, 1986
Member, Kansai Obstetrical and Gynecological Pathology Symposium, Recent Advances in Gynecological Pathology, Osaka, Japan, 1986
Member, Advanced Gynecologic Oncology, Harvard Medical School, Director, Georgetown Obstetrics and Gynecology Review Course, 1987, 1988
Member, Comprehensive Update in Obstetrics and Gynecology, Perinatal Resources, New York, 1986, 1987
Member, Symposium-Recent Advances in Sexually Transmitted Diseases, 26th ICAAC Seminar, New Orleans, 1986.
Member, Obstetrics and Gynecology Review, American College of Obstetrics and Gynecology, Dublin, Ireland, 1986
Member, Risk Factors and Alternate Treatments in Gynecologic Oncology, Italian Society of Gynecologic Oncology, Santa Margherita Ligure, Italy, 1986
Member, Gynecological Pathology Review Course, American Society of Clinical Pathology, Williamsburg, 1987
Member, Laser Surgery and Hysteroscopy in Gynecology Course,Virginia Beach, 1987-1990

Member, Emil Novak Memorial Course, Gynecology, Endocrinology, and High Risk Obstetrics, Johns Hopkins University, School of Medicine, Baltimore, 1987- 2002
Member, Emerging Technology and Future Trends in Clinical Laboratory Molecular Analysis, Scripps Clinic and Research Foundation, San Diego, 1988
Director, Short Course, Interpretation of Endometrial Curettings and Biopsies, International Academy of Pathology, 1988-1992
Member, Update in Surgical Pathology 1988,
Current Topics in Gynecologic Pathology, Washington Hospital Center, 1988
Member, International Symposium - Surgery in the Treatment of Gynecologic Cancer, University of Antwerp, Antwerp, Belgium, 1988
Member, The Italian Society of Gynecological Oncology and the EORTC-Gynecological Cancer Cooperative Group – The Conservative Treatment of Gynecological Malignancies, Santa Margherita Ligure, Italy, 1988
Member, 8th Annual Update in Obstetrics and Gynecology, University of Maryland, Annapolis, 1989
Member, American Society for Colposcopy and Cervical Pathology, Update on HPV Infection of the Female Genital Tract Symposium, 1989
Member, Annual Postgraduate Review Course in Obstetrics and Gynecology, University of California, San Francisco, 1989, 1990
Member, Comprehensive Review Course in Obstetrics and Gynecology, Georgetown University School of Medicine, 1989-present
Member, International Academy of Pathology, Long Course, Pathology of Reproductive Failure, Boston, 1990
Member, American Association of Pathologists, Symposium on Molecular Carcinogenesis, Boston, 1990
Member, Fourth International Symposium on Papillomavirus Infection and Genital Neoplasia, Chicago, 1990
Member, Review Course in Gynecologic Pathology, Magee-Womens Hospital, Pittsburgh, 1990
Member, ACOG-Advances Colposcopy Review Course, Jackson Hole, 1991
Member, 31st Annual Postgraduate Course in A Clinical and Histopathologic Overview of Obstetrics and Gynecology, New York, 1991 to present
Member, 47th Obstetrical and Gynecological Assembly of Southern California, Los Angeles, 1992
Member, Robert Meyer Symposium, Berlin, Germany, 1992
Member, ACOG-Advanced Colposcopy Review Course, Tucson, 1992
Member, California Society of Pathologists, Annual Meeting, San Francisco, 1992
Member, Orange County Ob/Gyn Symposium, Irvine, 1993
Member, University of Texas, Southwestern Medical Center at Dallas, Current Issues in Surgical Pathology, XII, 1993
Member, Organizing Committee, 12th International Papillomavirus Conference, Baltimore, 1993
Member, University of Iowa, Second Annual Review Course in Surgical Pathology, 1993
Member, The 4th Annual Review Course on Gynecologic Oncology and Pathology Matsumoto, Japan, 1993
Member, The Stanford University Current Concepts in Surgical Pathology Course, Stanford, California, 1994
Member, New York Symposium on Gynecological Cancer, New York, 1996
Member, Panel - Pathology of Incipient Neoplasia and Pathology of the Ovary, XXI International Congress of the International Academy of Pathology, Budapest, 1996
Co-Chairman, Panel - The Pathology of Pregnancy Related Conditions, XXI International

Congress of the International Academy of Pathology, Budapest, 1996
Member, 17th Annual Nation's Capital Advanced Gynecologic Surgery, Washington, D.C., 1997
Member, Surgical Pathology Review Course, Johns Hopkins University School of Medicine, 1997 to present
Member, Johns Hopkins-Humboldt University Joint Course in Surgical Pathology, Berlin, Germany, 1998
Director, Novak Memorial Course in Gynecological Pathology, Gynecology, Endocrinology and High Risk Obstetrics, Johns Hopkins University School of Medicine, Baltimore, Maryland 1993 – present
Director, Gynecologic Pathology Review Course, Johns Hopkins University School of Medicine, Baltimore, Maryland 1998 – present
Member, Pathology Education Course, Snowmass, Colorado, 1999
Moderator, International Society of Gynecological Pathologists Symposium on Endometrial Hyperplasia, New Orleans, 2000
Member, Surgical Pathology in the 21st Century, The University of Texas Southwestern Medical Center at Dallas, 2000
Co-Moderator – The Bethesda System for Reporting Cervical and Vaginal Cytology, Bethesda, Maryland 2001
Member, 3rd Joint International Workshop. Histologic and Cytologic Characterization of Human Tumors:Adjuncts in the Diagnosis, Prognosis and Clinical Monitoring Ischia, Italy, 2001
Member, Ovarian Cancer and High-Risk Women:Implications of Prevention, Screening and Early Detection, Magee-Womens Hospital, U of Pittsburg, 2002
Member, Fifth Annual UCSF and Stanford Current Issues in Anatomic Pathology, 2002, San Francisco, 2002
Member, Women's Cancer:Screening and Prevention, Inova Fairfax Hospital Cancer Center, Fairfax, 2002
Member, NCI Consensus Meeting on Ovarian Borderline Tumors, Bethesda, 2003
Member, Symposium on Ovarian Borderline Tumors, New Orleans, 2003
Member, California Society of Pathologists, 56th Annual Convention, San Francisco, 2003
Member, University Course – Gynecological Neoplasia and Cancer for Gynecologists, Pathologists, and Doctors in Training, Stavanger, Norway, 2004
President, Multidisciplinary International Conference on Gynecologic Cancer, Bologna, 2005
Moderator, International Society of Gynecologic Pathologists Symposium on Ovarian Borderline Tumors, Atlanta, 2006
Member, Surgical Pathology Evening Specialty Conference, USCAP meeting, Atlanta, 2006
Member, Course in Gynecologic Pathology of the Uterus, Aula Gemelli Instituti Biologici, Rome, 2006
Keynote speaker, 10th Panhellenic Congress of Obstetrics and Gynecology, Patras, Greece, 2006
Member, 1st International Ovarian Cancer Conference, Crete, Greece, 2006
Member, 11th Biennial International Gynecologic Cancer Society Meeting (IGCS): Satellite Symposium on Gynecological Tumor Pathology Honoring Professor Harold Fox, Loews Hotel, Santa Monica, CA, 2006
Moderator, International Society of Gynecologic Pathologists Symposium on Ovarian Cancer, San Diego, 2007
Moderator, Gynecologic Pathology Evening Speciality Conference, USCAP Meeting, 2008-11
Co-Director, Short Course Surface Epithelial Tumors of the Ovary, USCAP Meeting 2008-12
Co-Director, Ovarian Cancer Symposium. Elucidating Early Ovarian Carcinogenesis: Implications for Early Detection and Treatment. JHMI, Baltimore, MD, 2009
Course Faculty, 28th Annual Current Issues in Surgical Pathology, Dallas, Texas, 2009

Member, ASCP Gynecologic Pathology Course, Chicago, IL, 2009
Member, Symposium on Gynecologic Pathology, International Gynecologic Cancer Society, Prague, Czech Republic, 2010
Member, Evening Speciality Conference in Gynecology Pathology, USCAP, San Antonio, Texas, 2011
Member, Course in Gynecologic Pathology, Universita Cattolica del Sacro Cuore, Rome, Italy, 2011
Member, USCAP 2011 Diagnostic Pathology Update, Jackson Hole, WY, 2011
Member, Florida Society of Pathologists, 38th Annual Conference Anatomic Pathology, Orlando, 2012
Member, International Society of Gynecologic Pathologists USCAP Companion Meeting, Vancouver, March 2012
Member, Argentina Pathology Society Meeting, Buenos Aires, April 2012
Member, 6th Canadian Conference of Ovarian Cancer Research, Quebec City, Canada, 2012
Member, President's Symposium, The New York Pathological Society, New York, 2012
Member, Gynecological Pathology Symposium on Gestational Trophoblastic Disease, XXXIX Congress of the International Academy of Pathology, Cape Town, South Africa, 2012
Member, The 9th International Symposium on Advanced Ovarian Cancer: Optimal Therapy, Valencia, Spain, 2013
Course Director, 4th Annual Ovarian Cancer Symposium, Prevention and Early Detection of Ovarian Cancer, Memorial Sloane Kettering Hospital, May 2013
Member, Joint BAGP and ISGyP Meeting, Challenges in Gynaecological Pathology. June 27-28, London, 2013
Member, International Pathology Meeting: A Scientific and Scenis Tour of Sicily. Oct 6-13, 2013
Member, International Society of Gynecologic Pathology, Symposium Honoring Dr Robert E. Scully, San Diego, March 2014
Member, Endometriosis Foundation of America, 5th Annual Medical Congress, Politics, Ethics and Controversies: Endometriosis 2014, New York City, March 2014
Member, 5th Annual Ovarian Cancer Symposium. Prevention, Early Detection and Treatment, Toronto, September 2014

Invited Speaker:

State University of New York, Stony Brook Medical Center, Stony Brook, 1977
University of Chicago, Chicago, 1978
Pacific Coast Fertility Society, Scottsdale, 1978
Association of Clinical Scientists, Washington, D.C., 1978
International Society of Gynecologic Pathology, San Francisco, 1979
University of South Florida, Tampa, 1979
St. Louis Society of Pathologists, St. Louis, 1979
University of Utah, Salt Lake City, 1979
St. John's Mercy Medical Center, St. Louis, 1979
Walter Reed Army Medical Center, Washington, D. C., 1980
National Institutes of Health, Bethesda, 1980, 1984
Arthur Purdy Stout Society of Surgical Pathologists, New Orleans, 1980
Howard University School of Medicine, Washington, D.C., 1980
International Symposium on Human Testis Cancer, Mouse Teratocarcinoma and Oncofetal Proteins, Minneapolis, 1980
International Society of Gynecologic Pathology, Paris, 1980

George Washington University School of Medicine, Washington, D.C., 1981
Seattle Gynecological Society, Seattle, 1981
University of Pittsburgh, 1981
Madigan General Hospital, Tacoma, Washington, 1981
University of Washington, Seattle, 1981
Beth Israel Hospital, New York, 1982
Washington, D.C. Cytology Society, 1983
The Minnesota Obstetrical and Gynecological Society, Minneapolis, 1983
International Symposium of Gynecologic Pathology, Heidelberg, 1983
European Congress of Pathology, Hamburg, 1983
New York Pathology Society, 1984
International Society of Gynecological Pathologists, San Francisco, 1984
Tripler Army Hospital, Hawaii, 1984
American Academy of Dermatology, Washington, D.C., 1984
American Society of Microbiology, Symposium on Papillomaviruses, Las Vegas, 1985
UCLA Symposium on Molecular and Clinical Aspects, Plenary Speaker, Steamboat Springs, 1985
International Federation of Gynecologists and Obstetricians, West Berlin (FIGO), 1985
University of Cincinnati, 1985
Western Association of Gynecologic Oncologists, Keynote Speaker, Monterey, 1986
Colorado State Societies of Pathology and Obstetrics and Gynecology, Breckenridge, 1986
International Workshop on Papillomaviruses, Director of Workshop on Pathology for Molecular Biologists, Cold Spring Harbor, 1986
Interferon Therapy for Human Papillomaviruses Diseases Investigators Meeting, Research Triangle Park, 1986
Seventeenth Annual Seminar of the Nassau and Suffolk County Society of Pathologists, Special Guest Speaker, Gynecologic Pathology Slide Seminar, New York, 1986
ICAAC Symposium on Recent Advances in Sexually Transmitted Diseases, New Orleans, 1986
Yale University School of Medicine, New Haven, 1986
International Society of Gynecological Pathologists, Chicago, 1987
Texas A & M, 1987
Michael Reese Hospital, Chicago, 1987
Communitech, Cancer Progress II, New York, 1987
Veterans Administration Hospital, Washington, D.C., 1987
Felix Rutledge Society, Guest Speaker, Houston, 1987
University of California, San Francisco, Guest Speaker at Postgraduate Course, Current Issues in Anatomic Pathology, 1987
New York University Medical Center, Obstetrical and Gynecological Society, New York, 1987
Los Angeles Obstetrical and Gynecological Society, Los Angeles, 1987
The California Tumor Tissue Registry, 84th Semi-Annual Cancer Seminar on Gynecological Pathology, San Francisco, 1987
Society of Gynecologic Investigation, Baltimore, 1988
Downstate Medical Center, New York, 1988
University of Rochester, School of Medicine, 1988
University of Tennessee, School of Medicine, 1988
New Jersey Society of Pathologists, New Jersey, 1989
University of Maryland, 1989
Bringham and Women's Hospital, 75th Anniversary Celebration, Distinguished Alumni Pathology Symposium, 1989

Orange County Obstetrics and Gynecology Society, 1989
Long Beach Memorial Medical Center, 1989
The Memphis Society of Pathologists, 1989
St. Agnes Hospital, 1989
Maryland General Hospital, 1990
Franklin Square Hospital, 1990
National Taiwan University, Taiwan, 1990
Society of Gynecologic Investigation, St. Louis, 1990
Women's and Brigham Hospital, Boston, 1990
Memorial Sloan-Kettering Cancer Center, New York, 1990
Boston Obstetrical Society, Boston, 1991
International Society of Gynecological Pathologists, Chicago, 1991
American College of Obstetricians and Gynecologists, New Orleans, 1991
University of Pennsylvania, Philadelphia, 1991
German Society for Pathology, Friedrichshafen, Germany, 1991
University of Freiburg, Freiburg, Germany, 1991
Emory University, Atlanta, 1991
International Papillomavirus Meeting, Seattle, 1991, Plenary Speaker
Tampa Obstetrics and Gynecology Society, 1991
Washington Hospital Center, Washington, D.C., 1992
Greater Baltimore Medical Center, Baltimore, 1992
New York State Society of Pathologists, Tarrytown, New York, 1992
Freie University of Berlin, Germany, 1992
Washington Gynecological Society, Washington, D.C., 1992
San Francisco Gynecological Society, San Francisco, 1993
University of California, San Francisco, 1993
Stanford University, Palo Alto, 1993
American College of Obstetrics and Gynecology, Annual Meeting, Washington, D.C., 1993
American Society of Colposcopy and Cervical Pathology, Chicago, 1993
Yale University School of Medicine, New Haven, 1993
31st Annual Congress, Japanese Cancer Society for Cancer Treatment Meeting, Osaka, Japan, 1993
2nd Robert Meyer Memorial Symposium. International Society of Gynecological Pathologists and the German Division of The International Academy of Pathology. Recent Advances in the Pathology of Gynecologic Tumors made Possible by Molecular Biology. Weimar, Germany, 1994
Georgetown University, School of Medicine, Pathology, Grand Rounds, Washington, D.C., 1994
Connecticut Society of Pathologists, Farmington, Connecticut, 1995
Boston Obstetrical Society, Boston, Massachusetts, 1995
Tufts New England Medical Center, Boston, Massachusetts, 1995
New York Obstetrical Society, New York, New York, 1995
12th Annual Ella T. Grasso Symposium, New Haven, Conn., 1995
New Haven Obstetrical Society, New Haven, Conn., 1995
San Francisco Gynecological Society, San Francisco, California, 1996
Stanford University, Stanford, California, 1996
Georgetown University, Washington, D.C., 1996
Buffalo City Wide Ob/Gyn Grand Rounds, Buffalo, New York, 1996
Washington Society of Pathologists, Bethesda, Maryland, 1996
New York Pathological Society, Symposium on Gynecologic Cancer, 1996

Dept. Obstetrics & Gynecology, The Massachusetts General Hospital, Boston, Massachusetts, 1996
Symposium in Progress in Diagnosis and Treatment of Gynecological (Pre) malignancies, Vrije Universiteit Hospital, Amsterdam, 1996
Plenary Speaker, Austrian Society of Pathologists, Vienna, Austria, 1998
The South Bay Pathology Society, 47th Annual Spring Meeting, Monterey, California, 1998
University of Maryland Medical School, Baltimore, Maryland, 1998
12th Annual Symposium on the Long-Term Effects of Estrogen Deprivation, Los Cabos, Baja, California, 1998
IX World Congress on Gestational Trophoblastic Diseases, Jerusalem, Israel, 1998
American College of Obstetrics and Gynecology, Armed Forces District Meeting, San Antonio, Texas, 1999
XXVI International Symposium on Gynecologic Oncology, Barcelona, Spain, 1999
Yale University, School of Medicine, New Haven, 2000
Tri-State Pathology Society Meeting, New Orleans, Louisiana, 2000
Second Joint International Workshop. Histologic and Cytologic Characterization of Human Tumors: Borderline Neoplasia, Capri, Italy, 2000
The Austrian Society of Pathology, Vienna, Austria, 2000
University of South Florida, Tampa, 2000
Florida West Coast Association of Pathologists, Tampa, 2000
Michigan Society of Pathologists, Detroit, 2000
Michigan International Society of Gynecologic Pathologists, Atlanta, 2001
Australian Society of Colposcopy and Cervical Pathology, Perth, Australia, 2001
American Registry of Pathology, 25th Anniversary Scientific Symposium, Wash, D.C., 2001
Keynote Speaker, Pathological Society of Great Britain and Ireland, Liverpool, U.K., 2001
International Papillomavirus Conference, Florianopolis, Brazil, 2001
European Congress of Pathology, Berlin, Germany 2001
Dana-Farber/Harvard Cancer Center, Ovarian Cancer Symposium, Boston, 2001
Georgetown University School of Medicine, Wash DC, 2002
4th Biennial Ovarian Cancer Research Symposium, Swedish Medical Center, Seattle, 2002
Washington State Society of Pathologists, Skamania, Oregon, 2002
Phoenix Ob/Gyn Society, Phoenix 2003
Armed Forces Institute of Pathology, Washington DC, 2003
The National Cancer Institute "Regina Elena", Rome Italy, 2003
Australian Division of the International Academy of Pathology, 29th Annual Scientific Meeting, Sydney, Australia 2003
The San Antonio Society of Pathologists, 60th Annual Meeting, San Antonio 2004
The 9th Panhellenic Congess of Pathology, Kavala, Greece 2004
Los Angeles Society of Pathologists, George Kypridakis Memorial Lecture, 2004
Arthur Purdy Stout Society of Pathologist, San Antonio, 2005
The Fifth Panhellenic Congress on Gynecological Oncology, Athens, 2005
The Panhellenic Gynecologic Oncology Congress, Athens, 2005
The Croatian Society of Cytopathologists and Pathologists, Opatija, Croatia, 2005
Grand Rounds, Weil Medical College-Cornell University, New York, 2005
Grand Rounds, Georgetown University School of Medicine, Washington, D.C., 2006
Grand Rounds, New York University School of Medicine, New York, 2006
Keynote Speaker, Austrian Society for Pathology, Graz, Austria, 2006
South Bay Society of Pathologists, Slide Seminar, Monterey, California, 2007
Ob/Gyn Seminar sponsored by Quest Laboratories, Las Vegas, 2007

Keynote Speaker, Pacific Northwest Society of Pathologists, Portland, Oregon, 2007
Keynote Speaker, 4th Annual Meeting of the British Association of Gynaecological Pathologists, London, 2007
Colorado Society of Clinical Pathologists, Fourth Annual Stars in the Mountains Pathology Seminar, Vail, Colorado, 2007
Sacro Cuore-Don Calabria Hospital, Negrar-Verona, Italy, 2008
European Oncology Institute, Milan, Italy, 2008
St. Louis Society of Pathologists, 2008
American Society of Clinical Pathology, Baltimore, 2008
International Gynecologic Cancer Society, Bangkok, Thailand, 2008
7th Korea-Japan Gynecologic Cancer Joint Meeting, Seoul, Korea, 2008
American Association of Cancer Research, Symposium on Ovarian Cancer, Denver, 2009
The New England Pathology Society, Boston, 2009
The Shields Warren Lecture, 2009
The New England Pathology Society, 2009
Turkish Federation of Pathologists, Northern Republic of Cyprus, 2009
Helene Harris Memorial Trust 12th international Forum on Ovarian Cancer, Miami, Florida 2011
Keynote Speaker, Joint Annual Meeting, Swiss and Austrian Societies of Pathology, Feldkirch, Austria, 2010
Keynote Speaker, Wayne State University, Annual Gynecologic Oncology and Gynecologic Pathology Symposium, Detroit, 2011
University of Brescia, Brescia, Italy 2011
4th European Symposium on Ovarian Cancer, Reims, France, 2011
Keynote Speaker 61st New Jersey Society of Pathologists, Woodbridge, NJ, 2011
Los Angeles Society of Pathologists, Los Angeles, CA, 2013
Keynote Speaker, Pennsylvania Association of Pathologists, Harrisburg, PA 2013
Chicago Gynecological Society, Chicago, IL 2013
Session Chairperson and Speaker, Advances in Ovarian Cancer Research: From Concept to Clinic, American Association of Cancer Research, Miami, 2013
Keynote Speaker, 56th Meeting of the Gynecologic Oncology Society of Japan, Utsunamiya, Japan 2014
Joint Meeting of the German and Austrian Pathology Society, Graz, Austria, 2014
International Academy of Pathology, German Division, Bonn, Germany, 2016
European Division International Academy of Pathology, Cologne, Germany, 2016
Keynote Speaker,XXX1 International Congress of the IAP and the 28th Congress of the ESP, Cologne, Germany, 2016
Austrian Pathology Society, Velden, Austria, 2017
New York Medical College, Valhalla, New York 2017
Mount Sinai School of Medicine, New York, New York 2017

Publications:

Original Reports:

1. Ober WB, Sobrero AJ, **Kurman RJ** and Gold S: Endometrial morphology and polyethylene intrauterine devices. A study of 200 endometrial biopsies. Obstet Gynecol 1968; 32:7882-793.
2. **Kurman RJ**, Funk RL and Kirshenbaum AH: Spina bifida associated choristoma of mullerian origin. J Pathol 1968; 99:324-327.
3. **Kurman RJ** and Craig JM: Endometrioid and clear-cell carcinoma of the ovary. Cancer 1972; 29:1653-1664.
4. Herbst AL, **Kurman RJ** and Scully RE: Vaginal and cervical abnormalities after exposure stilbestrol in utero. Obstet Gynecol 1972; 40:287-298.
5. Herbst AL, **Kurman RJ**, Scully RE and Poskanzer DC: Clear cell adenocarcinoma of the genital tract in young females. Registry report. N Eng J Med 1972; 287(25):1259-1264.
6. **Kurman RJ** and Prabha AC: Thyroid and parathyroid glands in the vaginal wall. Am J Clin Pathol 1973; 59:503-507.
7. **Kurman RJ** and Scully RE: The incidence and histogenesis of vaginal adenosis. An autopsy study. Human Pathol 1974; 5:265-276.
8. **Kurman RJ** and Scully RE: Clear cell carcinoma of the endometrium. An analysis of 21 cases. Cancer 1976; 37:872-882.
9. **Kurman RJ** and Norris HJ: Mesenchymal tumors of the uterus. VI Epithelioid smooth muscle tumors including leiomyoblastoma and clear cell leiomyoma. A clinical and pathologic analysis of 26 cases. Cancer 1976; 37:1853-1865.
10. Leman MH, Benson WL, **Kurman RJ** and Park RC: Microinvasive carcinoma of the cervix. Obstet Gynecol 1976; 48:571-578.
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Grant Support:

Federally Supported:

NCI Contract - #NO1-CN-17501; Principal Investigator
The Pathology Reference Center for Evaluating the Effects of topical Retinoids on Cervical Dysplasia.
May 4, 1981 - June 3, 1986; $669,649.

NCI Subcontract - CN-35042-46; Principal Investigator
Epidemiologic Study of Black/White Differences in Breast Cancer Patient Survival Experience. June 15, 1984 - January 29, 1987; $137,395.

NCI Subcontract - Co-Investigator
A study of cervical fluid mutagenicity in relation to human papillomavirus infection, smoking and risk of cervical intraepithelial neoplasia. May 1986-87; $10,000.

NCI - 1 RO1 CA57550-01; Co-Principal Investigator
Human papillomaviruses and the pathogenesis of vulvar carcinoma.
July 23, 1992 - July 30, 1995; $797,247.
Ciba-Geigy - CGS-27421 Protocol 04 entitled, A Trial of Long Term Safety of E2-Matrix, A Matrix Estradiol Patch, in A Postmenopausal Population. February 1993 - December 1994 - $110,910.00.

NCI – Contract; Principal Investigator N01-CN-55159
Title: Randomized Trial on the Clinical Management of ASCUS and LSIL of the Uterine Cervix-Pathology Quality Control Group.
Period: 9/30/95-9/29/01
Direct Costs Awarded: $780,550
Indirect Costs Awarded: $159,245
Total Awarded: $939,795
Effort: 10%

Title: Pathogenesis of Ovarian Serous Carcinoma as the basis for Immunologic directed diagnosis and treatment
Period: 7/1/02-6/30/05
Direct Costs: $1,528,813
Indirect Costs: $970,799
Total: $2,499,612
Role/Effort: 5% Project 1 as co-investigator (Shih); 10% Core A as P.I.; total effort =15%

NCI – 1 RO1 CA116184-01A2; Principal Investigator
Title: Pathogenesis of Ovarian Serous Borderline Tumors
Period: 4/1/07-3/31/11
Direct Costs Awarded: $1,0008,288
Indirect Costs Awarded: $625,788
Total Awarded: $1,634,076
Effort: 20%

Department of Defense (DoD) -- W81XWH-11-2-0230; Principal Investigator
Title: Prevention of Ovarian High-Grade Serous Carcinoma by Elucidating Its Early Changes
Period: 09/30/2011 – 09/29/2016
Direct Cost Awarded: $9,600,285/ 5 years

Pharmaceutical Company Supported:

Upjohn Company - Protocol M5410/0293 entitled, The Effects of Postmenopausal Estrogen/PROVERA Hormone Replacement Therapy (HRT) on Endometrial Histology and Bone Mineral Density. August 1993 - April 30, 1995 - $314,540.00.

Clinical Research and Development, Wyeth-Ayerst Research Co. - HRT Study entitled, Hormone Replacement Study - Slide Review. September 1993 - August 31, 1998 - $59,825.

Randomized Trial on the Clinical Management of ASCUS and LSIL of the Uterine Cervix
Pathology Quality Control - Contract #No1-CN-55159 - September 30, 1995 - September 29, 2001 - $939,795

Merck - Human Papilloma Virus (HPV) Pathology Panel.
Study of Pilot Manufacturing Lot of HPV 16 Virus-Like Particle (VLP)
Vaccine in the Prevention of HPV 16 Infection in 16- to 23-Year-Old Females
(Protocol 005). 5/17/99-5/16/03 10% $ 274,360

Merck - Human Papilloma Virus Pathology Panel
Period: 5/17/99-5/16/03
Direct Costs Awarded: $226,743
Indirect Costs Awarded: $47,617
Total Awarded: $274,360
Role: P.I.
Effort: 10%

Watson Laboratories, Inc.
Title: Endometrial Biopsy Evaluations
Period:8/22/01-10/22/01
Direct Costs Awarded: $8,265
Indirect Costs Awarded: $1,735
Total Awarded: $10,000
Role: P.I.
Effort: 3%

Merck Protocol 013, sub-studies 011 and 012
Title: The F.U.T.U.R.E. I study (Females united to unilaterally reduce endo/ectocervical disease)
Period: 4/8/2004-2/28/2008
Effort: 20%
Role: P.I.
Direct Costs awarded: $1,108,511

Merck Protocol 015
Title: The F.U.T.U.R.E. II study
Period: 6/1/2004-12/31/2008
Effort: 20%
Role: P.I.

Direct Costs awarded: $686,895

MDS Pharma Services
Award Number: N/A
Title: Third Reviewer of Endometrial Biopsies on Pfizer Protocols 21810.02.03 and 04
Period: 7/1/01-12/31/06
Direct Costs Awarded: $20,593
Indirect Costs Awarded: $13,157
Total Awarded: $33,750
Role: P.I.
Effort: 2%

EXHIBIT B

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REFERENCES

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EXHIBIT C

Robert J. Kurman, M.D.

Past Deposition and Trial Testimony as Expert Witness (February 2015 – February 2019)

Elissa Powers, et al. v. Miami Beach Healthcare Group, LTD, d/b/a Aventura Hospital and Medical Center, et al., No. CACE-17-023085 (5), Florida Circuit Court, 17th Circuit Court, Broward County (October 31, 2018 – Deposition)

Gail Lucille Ingham, et al. v. Johnson & Johnson, et al., No. 1522-CC10417-01, Missouri Circuit Court, 22nd Judicial Circuit, St. Louis City (May 25, 2018 – Deposition)

Savannah Crews, Individually and on Behalf of Angela Dawn Hershman, deceased, et al. v. Johnson & Johnson, et al., No. 1422-CC09326-01, Missouri Circuit Court, 22nd Judicial Circuit, St. Louis City (June 16, 2017 – Deposition)

Eva Echeverria v. Johnson & Johnson, et al., No. BC628228, Superior Court of the State of California, County of Los Angeles (May 12, 2017 – Deposition)

Weidman J, et al. v. Hawaii Health Systems Corp., et al., No. 15-1-000166 KKS, Circuit Court of the Fifth Circuit, Hawaii (January 2017 – Deposition)

Gloria Ristesund v. Johnson & Johnson, et al., No. 1422-CC-09012-01, Missouri Circuit Court, 22nd Judicial Circuit, St. Louis City (March 21, 2016 – Deposition; April 25, 2016 – Trial)

Exhibit B

IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF NEW JERSEY

IN RE JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION	:	NO. 16-2738 (FLW) (LHG)
THIS DOCUMENT RELATES TO ALL CASES	:	

- - -

APRIL 2, 2019

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Videotaped deposition of ROBERT KURMAN, M.D. held in the offices of Duane Morris, LLP, 100 North City Parkway, Suite 1560, Las Vegas, Nevada, commencing at 9:26 A.M., on the above date before Pamela Cotten, CSR, RDR, Certified Realtime Reporter, Certificate No. 4497.

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Witness: ROBERT KURMAN, M.D.

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LAS VEGAS, NEVADA - TUESDAY, APRIL 2, 2019, 9:26 A.M.

VIDEO OPERATOR BROWN: Good morning. We are now on the record. My name is Darnell Brown, and I'm the videographer with Golkow Litigation Services. Today's date is April 2nd, 2019, and the time is 9:26 A.M.

This video deposition is being held in Las Vegas, Nevada, in the matter of In Re Talc for United States District Court, Eastern District of New Jersey.

The deponent is Dr. Robert Kurman.

Counsel, please identify yourselves for the record.

MR. DEARING: David Dearing from Beasley Allen for the plaintiffs.

MS. GARBER: Cynthia Garber, Robinson Calcagnie, for the plaintiffs.

MR. ROTMAN: Steve Rotman, Hausfeld, for the plaintiffs.

MR. BILLINGS-KANG: James Billings-Kang from Seyfarth Shaw, Personal Care Products' counsel.

MR. ANDERTON: Michael Anderton, Tucker Ellis, for PTI Royston and PTI Union.

MS. McBETH: Katherine McBeth, Drinker Biddle & Reath, on behalf of the Johnson & Johnson defendants.

MR. ZELLERS: Michael Zellers on behalf of the Johnson & Johnson defendants.

MS. AHERN: Hunter Ahern on behalf of Johnson & Johnson defendants.

VIDEO OPERATOR BROWN: The court reporter is Pam Cotten, who will now swear in the witness.

ROBERT KURMAN, M.D.,
called as a witness, and having been first duly sworn by the Certified Shorthand Reporter, was examined and testified as follows:

EXAMINATION

BY MR. DEARING:

Q Good morning, Doctor.

A Good morning.

Q We've met at least twice, I think. But I'm David Dearing. I represent the plaintiffs in this litigation, and I'm going to be asking you some questions.

You've been produced as an expert by Johnson & Johnson in this case. So, first of all, if you would, state your name, please.

A Robert Kurman.

Q What did you do to prepare for this

deposition?

A Well, you have to go back into my career. I guess, in a way, I've been preparing for a long time, so to speak.

I was a gynecologic pathologist for almost 40 years. And during the course of my career -- which involves teaching and research and clinical care, attending meetings, reviewing articles submitted to journals -- I would be constantly reading the literature in gynecologic pathology, which, of course, included ovarian cancer.

Q Can I just cut you off.

What have you done in the last ten days to prepare for this deposition?

A I've read over the defense -- the plaintiffs' gynecologic pathology expert and gone over papers that she's referred to. I've gone over my report and perhaps googled a few things here and there. Oh, PubMed, too.

Q Did you have meetings with Johnson & Johnson lawyers in preparation for this deposition?

A I did.

Q How much time have you spent with the Johnson & Johnson lawyers preparing for this deposition?

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A I didn't keep track of the meetings per se -- the time spent on the meetings per se.
Q Can you estimate.
A I hesitate not to estimate, since I'm under oath and I want to try to be as specific as possible.
Q One of the advantages of being an expert is you're allowed to estimate. So can you give me a ballpark? Was it ten hours?
MS. AHERN: Objection. Form.
THE WITNESS: Maybe 15.
BY MR. DEARING:
Q Have you billed them for that time yet?
A Some of it.
(The document referenced below was marked Deposition Exhibit 1 for identification and is appended hereto.)
BY MR. DEARING:
Q I'm going to hand you a composite exhibit, which I've marked as Exhibit Number 1. And it is your report, your CV, and your reference list and the appendixes -- appendices with your report. So feel free to refer to that as much as you need to.
I have copies for other people if anybody else wants a stack. I made six copies of everything. I hope we have enough.

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BY MR. DEARING:
Q So have you had a chance to just glance through what I just handed you?
A Yes.
Q Okay. And does that look like your report, your CV, your reference list, that kind of thing?
A Yes.
Q And did you write this report?
A I sure did.
(The document referenced below was marked Deposition Exhibit 2 for identification and is appended hereto.)
BY MR. DEARING:
Q Yesterday, I was given another document that I'm marking as Exhibit 2, and it's entitled "Defendants' Response to Plaintiffs' Document Requests Contained in Notice of Oral and Videotaped Deposition of Robert Kurman, M.D., and Duces Tecum."
Have you ever seen this document before?
MS. AHERN: Is that Exhibit 2?
MR. DEARING: It's Exhibit 2, yes.
THE WITNESS: This is what you showed me yesterday, isn't it? Is this what you showed me yesterday?
MS. AHERN: Go ahead and take a look through it. And if you recognize it, you can let him know.

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BY MR. DEARING:
Q It's okay if you haven't seen it; I just don't know.
MR. DEARING: I'll just hand them to you, Cynthia, and you give them to anybody who wants it.
MS. GARBER: I'll be your paralegal today.
MR. DEARING: Thank you. Then we can trade if you want.
THE WITNESS: No, I didn't see this.
BY MR. DEARING:
Q Okay. One of the things in this document that I just gave you, Exhibit 2, is a supplemental reference list, and it's the last four -- last three pages. It actually starts with page number 1 in the back of the document.
Do you see that?
A Yes.
Q And at the very top, there's a list of reports.
Do you see that list?
A Yes.
Q Those are all defense witnesses in this case, aren't they?
A Yeah, it looks that way.
Q Have you read all those reports?

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A No, I have not.
Q Any idea why they would be on your reference list if you haven't read them?
A They were offered to me, but I didn't read them all.
Q Have you read any of them?
A I did.
Q Which ones have you read?
A Dr. Michael Birrer, Dr. Jeff Boyd, Dr. Gregory Diette, Dr. Ie-Ming Shih, and Brooke Mossman.
Q And I think you mentioned that you read the report of Dr. Kane; right?
A I did.
Q A plaintiff expert?
A Yes.
Q Did you read any other report of plaintiff experts?
A No, I did not.
Q Have you relied on any other materials that aren't contained in your original reference list or this new reference list that I got yesterday?
A No, I have not.
Q And for clarity, did you prepare this reference list that was handed to me yesterday?
A I did not prepare that list.

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Q Did you ask someone to prepare that list?
A No, I didn't.
Q And the first time you saw it was this morning?
A You asked me about this originally. I said I didn't see it. Honestly, I didn't look at the last three pages.
Q Okay.
A When you mention that, I did see that before, the reference list.
Q Okay. But you didn't prepare it?
A But I did not prepare it, no.
Q Have you reviewed any internal corporate documents, emails, or testing data of Johnson & Johnson and Imerys?
A No, I haven't.
Q As I understand it, you are now a retired gynecologic pathologist; is that right?
A That's correct.
Q Congratulations.
A Thank you.
Q And I understand that your medical license has lapsed as well; right?
A I have a medical license in Nevada.
Q Oh, you do?

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A I do.
Q Do you agree with me that gynecologic pathology is not a recognized subspecialty of the American Board of Pathology?
A Gynecologic pathology is a -- an acknowledged subspecialty that we have in virtually all major institutions, but it is not a board specialty.
Q So you can't become board-certified in gynecologic pathology; correct?
A Well, the point is that, in order to do expert work in gynecologic pathology, you need to really train in it, as your plaintiffs' expert did. But you don't need specific board certification.
And, in fact, there was -- many years ago, there was -- and I was at the meeting. My predecessor at Hopkins, Dr. Don Woodruff, who was a gynecologist but had done a lot of gynecologic pathology -- in fact, he did the gynecologic pathology at Hopkins before I was there -- went to a meeting of the International Society of Gynecologic Pathologists and asked that it be made a board specialty.
And the pathologists resisted. They didn't want to do it. The reason being that they were concerned that people like Dr. Woodruff -- with all respect to him -- they didn't want gynecologists to be

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able to say they were board-certified. They wanted to completely compete it -- excuse me -- completely confine it to pathologists. So they didn't approve of having a board specialty.
Q But you can get board-certified in pathology; right?
A Oh, certainly.
Q Now, you've been deposed several times in this litigation; right?
A A few times, yes.
Q And you've actually testified in at least one trial; right?
A Yes. I think you were the person that --
Q It was me.
Have you testified in any other trials?
A No.
Q And each time you testified, you took an oath to tell the truth, the whole truth; right?
A Yes.
Q And did you do that?
A I did.
Q And do you still stand by the testimony you gave previously in this litigation?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I'd like to see what -- if

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you're referring to specifically, I'd like to see it. But I told the truth then, and I'm telling the truth now.
BY MR. DEARING:
Q Do you believe your report is a fair and balanced statement of the science on the issues that you address?
A I certainly do.
Q When you wrote your report in this case, who was your intended audience or your intended reader?
A I was responding specifically to the report of Dr. Kane, but I assumed that other individuals who were involved with this litigation would probably be reading it.
Q Did you write it thinking that the judge would read it?
A I assumed that that would eventually occur.
Q When you were first contacted by Johnson & Johnson regarding this talcum powder litigation, isn't it true that you had never researched the relationship between genital talc use and ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Are you referring to when I was initially contacted or for this specific MDL?
///

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BY MR. DEARING:
Q No. Before the MDL --
A Okay.
Q -- when Johnson & Johnson first came to you, at that time, you had not researched the issue of genital talcum powder use and ovarian cancer; right?
MS. AHERN: Objection. Form.
THE WITNESS: That's correct, because amongst -- in pathologists in the community and gynecologists, as far as I know, there was never a question that talc was involved with ovarian cancer, so there was no need for me to really pursue it.
BY MR. DEARING:
Q Well, when was that that Johnson & Johnson approached you to be a witness for them for the first time?
A It was about 2015.
Q So there was lots of literature out there and studies about the association or purported association between genital talc use and ovarian cancer; right?
MS. AHERN: Objection. Form.
THE WITNESS: They were epidemiology studies, which I think never rose to the level of being of interest to gynecologic pathologists -- gynecologic pathologists, for sure.

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BY MR. DEARING:
Q All those scientists that wrote those studies would be disappointed to hear you say that.
But there were also animal studies, weren't there?
MS. AHERN: Objection. Form.
THE WITNESS: Maybe. I don't know.
BY MR. DEARING:
Q There were also cell studies, looking at the effects of talc on -- on cell structures and cells --
MS. AHERN: Object.
BY MR. DEARING:
Q -- before Johnson & Johnson contacted you; right?
MS. AHERN: Objection. Form.
THE WITNESS: As I said, I didn't -- as you -- I didn't read the literature on it before, so I have no -- no idea.
BY MR. DEARING:
Q So when you -- I don't want to put words in your mouth.
Did you say that, before Johnson & Johnson contacted you, it wasn't important to you?
I don't remember what you said.
A I --

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MS. AHERN: Objection. Misstates.
THE WITNESS: I said before Johnson & Johnson contacted me, there was, in the gynecologic pathology community, never -- never a question of talc being involved with ovarian cancer. So, therefore, I wasn't doing research on talc and ovarian cancer.
BY MR. DEARING:
Q Based on the research you've done since Johnson & Johnson contacted you, you're aware that there are gynecologic pathologists who have published on this very topic, right, before Johnson & Johnson contacted you; right?
MS. AHERN: Objection. Form. Mischaracterizing the literature.
BY MR. DEARING:
Q William Welch at Harvard, for example, has published on this.
He's a gynecologic pathologist; right?
A I know Bill Welch quite well and --
Q I'm just using him as an example.
A Yeah, right. Right. In his -- he's on the paper, but I don't think he ever acknowledges that he says he supports talc as being a cause of ovarian cancer. I think he reviewed the pathology, and what his -- to make sure that these were whatever the

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authors were saying were ovarian cancers.
Q My point is, before Johnson & Johnson contacted you to be one of their experts, there was some interest among some gynecologic pathologists about this issue of talc and ovarian cancer, right --
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q -- as evidenced by the publications that they put their name on?
MS. AHERN: Objection. Form.
THE WITNESS: As I said, Bill Welch, who I honestly didn't speak to specifically about this topic, but I can -- at meetings, he's never brought it up. So I assumed -- assume.
I should say that, based on those publications, I -- he reviewed those cases. He said they were ovarian cancers, but I don't know if there's any evidence that he indicated that he believed that talc caused ovarian cancer.
BY MR. DEARING:
Q And you understand I'm not talking about just Dr. Welch.
I'm talking about other gynecologic pathologists have contributed to papers, studies on the issue of talc and ovarian cancer before Johnson &

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Johnson came to you and hired you as an expert; right?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Are you aware of those papers?
A You'll have to show them to me.
Q Okay.
A Please.
Q Okay. So none come to mind, as we sit here?
A You'll have to show them to me.
Q Okay. And would you also agree that, before Johnson & Johnson hired you, many other scientists in other fields were quite interested in the issue of genital talc use and ovarian cancer and were publishing on it?
MS. AHERN: Objection. Form.
THE WITNESS: As I said, since I did not research the area of talc use and the possible talc exposure to the development of ovarian cancer prior to the time that Johnson & Johnson contacted me, I wasn't aware of those studies.
BY MR. DEARING:
Q All right. But since then, since you've been hired by Johnson & Johnson, you've done a lot of research on it and you've seen that studies were published long before Johnson & Johnson hired you, even

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as far back as the '70s, on this very topic; right?
A I've seen, since my research on the subject, yes, that there have been studies that were performed before 2015.
Q And you've never published on the topic of talc and ovarian cancer; correct?
A No, I have not.
Q And you've never lectured on it?
A I have never lectured on it.
Q Have you ever studied talc, and specifically Johnson & Johnson's baby powder or Shower to Shower product, under a microscope?
MS. AHERN: Objection. Form.
THE WITNESS: I have not specifically done a study looking at talc exposure in tissues under the microscope.
BY MR. DEARING:
Q Have you even looked at just plain talc under a microscope?
A Not specifically, no, I have not.
Q Have you looked at it nonspecifically?
What do you mean by that?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q When you say "not specifically," what do you

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mean?
A Well, there may -- if there was a study that had -- if there was some kind of exposure to talc that I was looking under the microscope, I would assume that it would -- that it would create a foreign-body giant cell granulomatous inflammation. And I would, therefore, have polarized it, perhaps looked at that that way. But it haven't seen that.
MR. DEARING: Okay. Move to strike as nonresponsive.
BY MR. DEARING:
Q My question is, have you looked at talc or Johnson & Johnson body powder products under a microscope?
A I have not looked at talc, Johnson & Johnson products, as far as I know, under the microscope.
Q Have you ever studied gynecologic tissue -- I'm sorry. Strike that.
Have you ever studied talc in gynecologic tissue under a microscope, you specifically?
A I thought I just answered that question. Isn't that what you just asked me?
Q No. I asked if you looked at the powder. Now I'm asking you about tissue.
A Oh. So your first question was talc powder

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not being in tissue?
Q Right. My first question didn't mention tissue at all.
Do you need me to ask it again?
A Well, certainly. I don't look at -- I look at tissue. I never look at things that are not tissue.
Q Okay. You don't think it's important to look at the morphology and characteristics of talc by itself in order to assist you in looking at talc in tissue?
A No. If I see it in tissue, I'd recognize it, as I mentioned with polarization. Seeing a foreign-body giant cell reaction, polarizing it there, seeing birefringent particles, might be talc.
Q Have you studied talc in gynecologic tissue under a microscope?
A Okay. So now we are talking about tissue.
Q Yeah.
A I have not.
Q And you just said that you could look at talc in tissue and recognize it by polarized light.
Isn't it true that you hardly ever do that?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q In fact, I think those were your actual words, that you hardly ever do that.

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A Well, let me describe the situation to you. I don't routinely look at tissue using polarized light. There's got to be an indication.

The indication is, do I see a foreign-body giant cell reaction? Then I would say, "Ah, there may be something here that's polarizable." Then I would polarize it.

Q That doesn't happen very often, does it?

A It does not happen very often.

Q Have you ever participated in any lab study of cellular reaction to talc exposure?

A I haven't --

MS. AHERN: Objection. Form.

THE WITNESS: I have not participated. I'm not a laboratory scientist. I'm not a bench scientist. I'm a surgical pathologist.

BY MR. DEARING:

Q And you're not qualified to perform analytical scanning electron microscopy or transmission electron microscopy or Raman spectroscopy, are you?

A Those techniques are not those -- I don't use those techniques.

Q You've served on many peer review and editorial committees for a variety of journals and professional publications.

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Can you describe how that peer review process typically works?

A Sure. Paper's submitted to a journal. The editor looks it over and determines, among the people on the editorial board or people not necessarily on the editorial board, who has the necessary expertise or interest in the area to review the paper and provide a commentary on it, pointing out whether the paper is acceptable as submitted or are there problems with it that need to be addressed by the authors.

So that reviewer then submits a report back to the editor. The editor reviews it, looks at it, one reviewer's comments -- and invariably it is sent to more than one reviewer -- and compares the review of one reviewer to the review of another.

If they're concordant the editor, based on that editor's judgment, would probably agree and say, based on these reviewers' comments, I will either accept the paper, I will reject it out of hand, or I will resubmit it to the authors and say it's -- the reviewers have deemed that your paper is acceptable with the provision that you address certain specific issues. And those issues are listed for the -- for the author to look at.

And the author reviews those comments and then

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decides how to respond to those comments. And then that's resubmitted to the -- to the editor. And then the editor, again, makes a decision. Did these authors provide enough explanation to now have successfully addressed the concerns of the reviewers? Or, hmm, maybe not, in which case they might send it back to the reviewers and ask them again to review the paper.

And it goes through the same process again of the reviewers saying, well, yes, they have addressed the questions, or, no, they haven't addressed the questions and, therefore, again submit their recommendation to the editor.

Q And that's been your experience and your own participation either by submitting general publications for publication or serving on these review committees?

A Yes.

Q And would you agree that the primary purpose of the peer review process is to validate proposed scientific findings, methodologies, opinions, and hypotheses so that bad science doesn't get published in journals?

MS. AHERN: Objection. Form.

THE WITNESS: The responsibility of the reviewers is to perform a fair review of the science and determine whether that science has been -- is

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appropriate -- is reliable, is valid, and, therefore, agree or disagree, as I said earlier, to either reject or accept the paper.

BY MR. DEARING:

Q None of the opinions that you're offering today regarding talc and ovarian cancer have ever been published or have ever gone through any peer review process, have they?

A That's correct.

Q Have you tried to publish your opinions about talc and ovarian cancer?

A No, I have not.

Q When Johnson & Johnson first approached you for serving as an expert witness in the MDL litigation that we are here about today, what's your understanding of what they wanted you to do?

A Well, it was my impression from speaking with them that the primary -- what my primary function was, really, was to be an expert in gynecologic pathology, which I am, I think, and go over the issues of ovarian carcinogenesis from the standpoint of surgical pathology and to review the data concerning talc exposure and possible involvement in the development of ovarian cancer in terms of ovarian carcinogenesis causation and to review the plaintiffs' expert

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gynecologic pathologist's report.
Q And when you say "review the data," are you talking about cell study data or are you talking about epidemiology? What are you referring to?
A Well, specifically -- not epidemiologic data because I testified to that before, but I'm not an epidemiologist. So it was -- really, the interest was in my expertise in gynecologic pathology with the focus, again, being on the -- my work as a gynecologic pathologist. As I said, I'm not a bench scientist. I can certainly review some of those papers, but my area and expertise is surgical pathology.
Q Is it fair to say that, if there are studies out there pertaining to talc and ovarian cancer that are not on your reference list, that you've not reviewed them?
MS. AHERN: Objection. Form.
THE WITNESS: I may have seen other papers that I've looked at but didn't decide, for whatever reason, to specifically -- there's a huge -- you know, there are a lot of papers out there that I may have even missed. So there may be some things out there that I'm not aware of that I didn't include.
BY MR. DEARING:
Q Since epidemiology is not your specialty, is

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it fair to say that you've not considered the complete body of literature in epidemiology on the issue of talc and ovarian cancer?
A No, no, I wouldn't say that at all. I've looked at those epidemiology papers, and even though I'm not an epidemiologist, I can get a -- I can understand them. I'm not an expert in epidemiology, but their papers are important, and I reviewed them.
Q Right. And if you reviewed them, are they identified on your reference materials list, either the first one or the one I got yesterday?
A I imagine that some of them are. I'd have to look specifically.
Q Okay. Well, I didn't see any epidemiology studies on the first list I was provided with your original report. You're welcome to look at it. It's right in front of you. But does that sound right? I'm not going to spend a lot of time on it.
MS. AHERN: Are you talking about his reference list from his report?
BY MR. DEARING:
Q Right. I didn't recognize any epidemiology studies --
A Well, I'd have to go through the reference list and look at them, actually. Can I do that?

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Q Sure. There are several on the second one that I got yesterday, but right now I'm asking you about the first one.
A Okay. Well, for starters, Camargo, I believe, may have been an epidemiologic study.
Q Can you refer me to what page?
A Oh, I'm looking at page 12 of the references, Number 9, Camargo.
Q Okay.
A There are a couple of papers by Dan Cramer, 14 and 15, which are epidemiologic studies, one -- 15, in fact, was published in an epidemiology journal.
Number 23, Falconer in "Ovarian Cancer Risk After Salpingectomy: A Nationwide Population-Based Study."
Q Let me ask a question in a different way, if I can.
A Okay.
Q Certainly lots of these studies rely on population data.
Did you rely on any of the population data or findings of epidemiology studies in preparing your report and the opinions within your report?
A Well, as I've said, I've indicate I -- earlier on in the litigation, I have reviewed -- I reviewed

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many of these studies, the epidemiologic studies. I briefly looked at them again -- over again and didn't see any reason that they brought -- changed my testimony from what I've done in the past.
So, yes, I have looked at them and I've taken them into account.
Q Do you think you have reviewed epidemiology studies on this topic of talc and ovarian cancer that aren't reflected in your reference list?
A I may have, yes.
Q Have you reviewed the Terry study?
A Terry study, no, does not sound familiar.
Q Have you reviewed the Taher study, T-a-h-e-r?
A I'd have to see that one. I might have. Do you have it?
Q I do. We're going to come back to it in a little bit. I'm just trying to get a --
A At this point, I won't comment. I'd like to see it. I may have.
Q You may have?
A Yeah.
Q How about Penninkilampi? Have you looked at that study?
A I looked at the abstract.
Q On page 12 of your report -- and I think you

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sort of just said this -- you say that "Although Dr. Kane offers opinions in a host of areas outside of her field, including epidemiology and cancer biology, I will focus my report on the primary area of" --
A Excuse me. Could you tell me exactly where you are reading from?
Q Sure. Page 12.
A Yeah, I got that.
Q At the top. First paragraph.
A Okay.
Q Last sentence.
A Okay.
Q "Although Dr. Kane offers opinions in a host of areas outside her field, including epidemiology and cancer biology, I will focus my report on my primary area of expertise, gynecologic pathology."
So I want to ask you about that statement.
Does that mean that you only intend to testify about gynecologic pathology, and not epidemiology and cancer biology?
MS. AHERN: Objection. Form. Depends what you ask him.
MR. DEARING: He seems to be defining the

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parameters of his testimony. So I want to know what he's comfortable with testifying about.
MS. AHERN: Understood.
THE WITNESS: As I said, that is my primary focus. An epidemiology study that may touch on it briefly, I could mention, but it isn't what I'm focusing my specific testimony on.
BY MR. DEARING:
Q So, as you sit here today, it is not your intention to dissect epidemiology studies?
A That's correct.
Q And it is not your intention to offer testimony on cancer biology?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Right?
A That's correct.
Q Does your report contain a complete outline of your opinions?
MS. AHERN: Objection. Form.
THE WITNESS: What do you mean by a "complete outline" of my opinions?
BY MR. DEARING:
Q Does your report contain a complete statement of your opinions regarding talc and ovarian cancer?

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MS. AHERN: Objection. Form.
THE WITNESS: Pretty much so, yes.
BY MR. DEARING:
Q Are you intending to offer any opinions that are not contained in your report?
MS. AHERN: Objection. Form.
THE WITNESS: I'd have to hear the question, but I don't think I would.
BY MR. DEARING:
Q Was it your idea to add the 16 defense experts to your second reference list -- 16 expert reports?
A No.
MS. AHERN: David, can I just quickly -- it might help a little bit. We put together the reference list which contains any materials we provided to him, should he want to review them, and also includes articles I think he found himself that he's reviewed.
So we tried to give you a complete list of everything that he had to consider. You'll have to ask him if he actually reviewed it.
BY MR. DEARING:
Q The only plaintiff expert report you reviewed was Dr. Kane's; right?
A Correct.
Q Are the opinions of the other defense experts

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in this case relevant to your pathology opinions?
A Well, I didn't read them. So I can't comment on them.
Q But if you thought they were relevant, you would have read them; right?
A Since they weren't pathologists and my focus was on the pathology, I -- I would think that's correct. I would focus on pathology.
Q Certainly your pathology opinions are not dependent on the opinions of the other defense experts; right?
A Well, again, I'd have to see -- if you're referring to something specifically, I would like to see what it is. But, in general, they're not -- it's not focused -- if they don't discuss pathology, it is not relevant to my testimony.
Q Since your report was written long before yesterday when I received your supplemental reference list, is it fair to say that none of the opinions in your report are dependent upon anything that's on the reference list that I was provided yesterday?
A That's correct.
Q Do any of the materials I was recently provided on your second reference list influence or affect or change any of the opinions that you've

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already put in your report?
A Let me look at that reference list again.
Well, I don't know if I mentioned it. I did read -- oh, I did mention it earlier. I read Dr. Shih's deposition, and it included a report of his, a study he was doing. I read that. But I mentioned that before.
Other than that, no. I mean, obviously, the Jeff Seidman study, I was an author. I'm involved with that paper on papillary tubal hyperplasia. I wrote it, so I know that.
I would say, yes, actually, looking at it, there was an important paper that is listed on page 2 -- important in my opinion -- by -- it is the second one from the top. Ducie, H. et al., which I would -- it's not in my original report, but I would -- I might refer to that.
Q I believe the question was did your review any of the materials on the supplemental reference list affect or change any opinions --
A Oh.
Q -- you've already written in your report?
A No, it does not change my opinion.
Q If you are not intending to offer epidemiology opinions or discuss the underlying data of epidemiology

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studies, why did you add about 15 epidemiology studies in your supplemental list for today's deposition?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Or was your testimony you didn't add those; someone else did?
A Yes.
Q Okay.
A They were provided to me. If I was of interest to read them, I could read them. But I didn't read them.
Q Okay.
A I did mention I did look at the abstract of Penninkilampi.
Q Do you think you read any of the epidemiology studies that are in the supplemental list?
A Let me take a look.
MS. AHERN: You mean recently or previously?
BY MR. DEARING:
Q They're in a reliance list. So did you read any anticipating you might review on them?
MS. AHERN: Well, I would object to the characterization this is a reliance list. This is a supplemental list of materials that we either provided to him or he selected himself so that you had full

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disclosure of what he might have reviewed in preparation for the deposition. We were just overinclusive.
MR. DEARING: Thank you.
BY MR. DEARING:
Q Did you read any of these studies that are on the supplemental list?
A Again, as I mentioned --
Q You read one of them, but --
A -- in the past when I did discuss epidemiology in greater detail, I have read Gates, Gertig. Gonzalez, I actually might have looked at more recently. Houghton, I've looked at in the past. I mentioned Penninkilampi.
Q Are you prepared to discuss those studies today?
A Well, as I said, I looked in the past I haven't really recently gone over them in depth. If there's some specific question you may want to ask, I could look at it. But the focus of my testimony is not on the epidemiology, as we've discussed.
Q I want to try today to keep you within your field of expertise, and I don't want to drag you out in any other area that you're not comfortable in or you don't feel qualified in. So if I do that, please tell

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me. Okay?
A Okay.
MS. AHERN: Objection.
BY MR. DEARING:
Q Based on your research that you've done in your entire career, both before and after Johnson & Johnson hired you as an expert in this case and in this litigation, in general, years ago, would you agree with me that there are about 30 or so epidemiology studies on talc and ovarian cancer that are not on either of your reference lists?
MS. AHERN: Objection. Form.
THE WITNESS: I'd have to go over and look all these 30 that you mentioned. So I can't really comment.
BY MR. DEARING:
Q As you sit here now, would you agree that your two reference lists do not include all of the epidemiology studies, not even all the meta-analysis studies, on talc and ovarian cancer?
A That is correct.
Q And that's because either you weren't aware of them or you read them and didn't find them compelling or the attorneys didn't put it on the list for you to review; right?

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MS. AHERN: Objection. Form.
THE WITNESS: Yeah, could you please --
MR. DEARING: Sure.
THE WITNESS: -- rephrase your question.
BY MR. DEARING:
Q So there are quite a few epidemiology studies and meta-analyses on talc and ovarian cancer that are not on either of your reference lists.
A That's correct.
Q Ms. Ahern just said on the record that they provided you the reference list.
MS. AHERN: Objection. Form. The supplemental reference list is the one that we put together.
MR. DEARING: Okay.
BY MR. DEARING:
Q If there are epidemiology studies that are not on your original reference list -- let me ask you: Did you put together your original reference list?
A Yes.
Q Did the lawyers help you do that?
A Not really. It was me.
Q Okay. The original reference list has a handful of epidemiology studies that we started to go through.
A Yes. We were only up to like page 2. There

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may have been more.
Q Right. But it's your list?
A Yes.
Q You wrote it. You made it.
A Yes.
Q You know there are quite a few epi studies that are not on that list; right?
MS. AHERN: Objection. Form.
THE WITNESS: That is correct.
BY MR. DEARING:
Q And there are quite a few that aren't on the list you made, and there are quite a few that still aren't on the list that the lawyer made, the supplemental list; right?
A Please rephrase your question.
Q Sure.
Whatever reason, your reference list does not include quite a few epidemiology studies; right?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q We've already established that.
A We said that, right.
Q The second list that I got yesterday also excludes quite a few epidemiology studies, including several meta-analysis studies.

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Do you agree with that?
MS. AHERN: Objection. Form.
THE WITNESS: That is correct.
BY MR. DEARING:
Q Now, because you didn't prepare the second list, the lawyers did, and the fact that some of those large studies are not on this list, do you interpret that to mean they didn't provide those to you or didn't think you should look at those?
MS. AHERN: Objection. Form.
THE WITNESS: I don't know what the -- what the reason was why they weren't included on that list.
BY MR. DEARING:
Q Before we get too far into the pathology weeds today, I want to ask you just some basic questions to make sure we're communicating well, like some definitions.
For example, if I use the term "biologic plausibility," can you tell me what that means to you? Or does it mean anything to you?
A It means something to me. I think it's a factor that would be very important in establishing causation. So the way I interpret -- view it is that it's -- biologic explanations often, really, base cellular studies or extracellular studies that could be

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incorporated with the human population studies to seem to go together in supporting a particular argument.
Q Are you familiar with the nine Bradford Hill considerations that are used to assess the strength of proposed causal associations?
MS. AHERN: Objection to form.
THE WITNESS: I'm familiar with the Bradford Hill criteria, yes.
BY MR. DEARING:
Q Are you familiar with the biologic plausibility consideration of the Bradford Hill assessment?
A That's what I just explained, I thought.
Q Okay. That's what I'm asking you. I wanted to know is that your interpretation of the Bradford Hill criteria or assessment, or is that your, Dr. Kurman's, definition of biologic plausibility?
MS. AHERN: Objection. Form.
THE WITNESS: That's my interpretation, which is what I believe is the criterion spelled out by Bradford Hill.
BY MR. DEARING:
Q In the term "biologic plausibility," as you've just described it, how do you define "plausibility"?
A I thought I just described it.

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Q Well, tell me what you mean by plausibility.
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: I -- that's -- "plausibility" is a very general term. Bradford Hill describes not plausibility but biological plausibility, and that's what I just said a minute ago is my definition, which I thought was an interpretation of the way Bradford Hill used it.
BY MR. DEARING:
Q To you, is there a difference between biologic plausibility and biologic probability?
MS. AHERN: Objection. Form.
THE WITNESS: I don't know exactly what biologic probability is. I would stick with biologic plausibility.
BY MR. DEARING:
Q Does biologic plausibility have any application to pathology?
A I think pathology studies could be used for evidence of biologic plausibility in the application of the Bradford Hill points.
Q Right. Bradford Hill is a epidemiology causation assessment tool; right?
A Correct.
Q Right. And you've already said you're not

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here to talk about epidemiology specifically; right?
MS. AHERN: Objection. Form.
THE WITNESS: I -- that's what I said.
BY MR. DEARING:
Q Okay. So I'm trying to determine whether the term "biologic plausibility" has any application to you outside the field of epidemiology.
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: As I mentioned, this litigation is about causation, does talc cause ovarian cancer.
And what virtually everyone agrees is, in order to come to a conclusion that it does, is to apply the Bradford Hill criteria, of which biologic plausibility is one among several that could go along to support causation.
So in that regard, that's the way I'm interpreting and using "biologic plausibility."
BY MR. DEARING:
Q Do you agree that, in order to establish causation, you do not have to satisfy all nine of the Bradford Hill considerations?
A I think that's correct, yes.
Q I want you for this question, if you would, to step out of the world of epidemiology and Bradford Hill and just tell me, from a pathologist standpoint, what

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does the word "plausible" mean to you?
MS. AHERN: Objection. Form.
THE WITNESS: We never use the term "plausible" --
BY MR. DEARING:
Q Okay.
A -- in -- in pathology.
Q Okay.
A I've never --
Q So anytime that word "plausible" or "plausibility" comes up today, you're going to be discussing it in terms of epidemiological definitions, or are you going to use it some other way?
MS. AHERN: Objection. Form.
He's giving you his definition, which is not an epidemiologic deposition per se.
MR. DEARING: I object. That's not true. For one, he keeps referring back to what is in the Bradford Hill criteria. I don't know what his definition is.
MS. AHERN: You keep defining Bradford Hill criteria as epidemiology. It's not. I think that's the confusion here.
MR. DEARING: Let's ask. Let me ask him. Okay. I don't need your commentary, but thank you.
BY MR. DEARING:
Q I believe you just testified that the

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definition you were giving of "biologic plausibility" was what's offered in the Bradford Hill assessment; is that right?
A That's correct.
Q Okay. Is that also your definition?
A That's what I said.
Q Okay. And you don't have any other definition of "plausibility" other than the way it is interpreted and defined as part of the Bradford Hill assessment?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said, and I'll repeat it, that -- in this litigation, we're attempting to determine whether talc causes ovarian cancer. The -- everyone seems to agree that the Bradford Hill criteria is the way to establish that. One of those criteria is biologic plausibility.
My definition of "biologic plausibility" is the biologic plausibility that Bradford Hill uses in his several points.
BY MR. DEARING:
Q And you've articulated that to the best of your ability already?
A Yes.
Q As part of your methodology that you employed in arriving at your expert opinions regarding talcum

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powder and ovarian cancer, did you assess whether it is biologically plausible for talcum powder to cause inflammation?
A Talcum powder can cause inflammation.
Q Did you consider biologic plausibility that talcum powder could cause inflammation that might be a precursor to cancer?
A For starters, I think it's very important to look at chronic inflammation. I've noticed that people tend to throw that around. "Chronic inflammation" is a very broad term.
In terms of the talc exposure, it really refers to a very specific subtype of chronic inflammation -- I alluded to it earlier -- namely foreign-body giant cell granulomatous inflammation. And that, in my opinion, has not been shown to be associated with ovarian cancer.
Q So are you saying the only type of chronic inflammation that might contribute to causing ovarian cancer is the giant cell granuloma-type inflammation?
A No, no.
MS. AHERN: Objection to form.
THE WITNESS: That's not what I said.
BY MR. DEARING:
Q Okay. Can you repeat what you just --

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A Sure.
Q -- tried to explain.
A I said that chronic inflammation is a very broad term. And in the context of this litigation, specifically does talc cause ovarian cancer, talc causes a very specific -- or I should say induces a very specific type of inflammation, which is referred to as foreign-body giant cell granulomatous inflammation. And that type of inflammation is not associated with ovarian cancer.
Q How do you know that talc used in body powders elicits that kind of inflammation that you just described, giant cell granuloma inflammation?
A Well, talc is what's -- what I'm referring to. In the literature, talc has been used in a variety of situations where it's caused foreign-body giant cell granulomatous inflammation.
Q What are some examples of those situations where talc caused that?
A Pleurodesis.
Q Okay.
A Contamination from gloves.
Q Right.
A That would be the -- well, sometimes it's been seen in creating skin granulomas. I remember one case

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that I ran across that a woman used a -- an antiperspirant that contained talc, and she got a skin -- a granuloma in her axilla. That would be about it.
Q Giant cell granulomatous inflammation is hardly -- is virtually never seen in gynecologic tissue; right?
A Very, very rare is it -- is it seen, that's correct.
Q Is it your testimony that the giant cell granulomatous inflammation is the only kind of inflammation that might be a precursor for cancer?
MS. AHERN: Objection. Form. Misstates his testimony.
THE WITNESS: I didn't say that at all.
BY MR. DEARING:
Q Okay. What other type of chronic inflammation might be a precursor for cancer?
MS. AHERN: Objection. Form.
THE WITNESS: In my opinion, inflammation very rarely initiates cancer. It can be seen certainly in association with cancer, but it's usually -- it typically occurs later in the whole process of malignancy.
///

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BY MR. DEARING:
Q And in that statement, when you use the term "inflammation," are you talking giant cell granulomatous inflammation, chronic inflammation, or something else?
A I'm --
MS. AHERN: Objection. Form.
THE WITNESS: I'm not talking about foreign-body giant cell granulomatous inflammation, which, as I said earlier, I don't see any evidence of causing ovarian cancer.
So when I was referring in a more general statement to respond to your question about chronic inflammation, I was referring to chronic inflammation of a different type.
BY MR. DEARING:
Q Okay. You first said when we started talking about inflammation, that it's very important to make sure we're talking about the same kind of inflammation, because they are different types; right?
A That's correct.
Q That's why I'm trying to be very specific about this.
Are you aware of any other types of chronic inflammation, other than giant cell or granulomatous

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inflammation, that can cause cancer?
MS. AHERN: Objection. Form.
THE WITNESS: We're really talking about, again, my testimony specifically concerned with ovarian cancer. So I'm not talking about pancreatic cancer, lung cancer, stomach cancer.
I mean, cancers are all different, and I'm not going to stand up and tell you -- respond to that question because it's a very general question.
BY MR. DEARING:
Q I thought it was a very specific question.
There -- you discuss in your report essentially two types of inflammation -- chronic inflammation, infectious chronic inflammation and noninfectious; right?
MS. AHERN: Objection. Form.
THE WITNESS: That's one type.
BY MR. DEARING:
Q That's two types.
A Well, two types.
Q Okay. Are there any other types of chronic inflammation?
A Just general chronic inflammation not associated -- well, infectious or noninfectious, right.
Q Okay. So breaking inflammation down, there's

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two broad types, either infectious or noninfectious; right?
MS. AHERN: Objection.
Are you talking about foreign body, or are you talking about general inflammation?
THE WITNESS: Right. Foreign-body giant cell reaction is a type of -- type of inflammation that can be either infectious or noninfectious. But it's different than other types of chronic inflammation, which may be infectious or noninfectious.
BY MR. DEARING:
Q What's your understanding of the plaintiffs' experts' explanation for how talc causes chronic inflammation which can cause ovarian cancer?
A You're specifically referring to Dr. Kane?
Q Well, it's not just Dr. Kane's position, is -- well, you probably haven't read all the other plaintiffs' positions.
So as you understand it, based on whatever you've looked at, what's your understanding of that mechanistic process?
A I believe it's unreliable and invalid.
Q No, I don't want your commentary. I want what do you understand that the plaintiffs' experts are alleging.

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MS. AHERN: Objection. Form.
THE WITNESS: I haven't read the other experts, as you yourself pointed out. I've read Dr. Kane's explanation. And, as I said, her explanation, I believe, is invalid and unreliable.
BY MR. DEARING:
Q So as you sit here today, you have no idea how the plaintiffs, through their experts, are alleging talc causes ovarian cancer?
A I didn't --
MS. AHERN: Objection. Form.
THE WITNESS: Excuse me. I've interrupted you.
I didn't read those expert reports. I don't know what they said.
BY MR. DEARING:
Q I know you haven't read the reports, but are you saying that you don't know what the plaintiffs' experts are alleging as a mechanistic process of how talc causes ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: How would I know if I can't read the reports? I don't know what they said.
BY MR. DEARING:
Q What's your understanding of Dr. Kane's opinion on how talc causes ovarian cancer?

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A I just told you. I said I thought it's invalid and unreliable.
Q I'm not asking you for what you think of it. I'm asking you what's your understanding of what she is saying.
How does she describe the mechanism of how talc causes ovarian cancer?
A Well, why don't we go through her report, and I can discuss those with you.
Q You don't remember?
A I want to go through them so we get them absolutely right.
Q I'll come back to it --
A Okay.
Q -- because that's a big part of this.
A Okay.
Q I just wanted to know what you remembered.
A Okay.
Q Is it your opinion that the notion that talc can cause chronic inflammation, which can cause ovarian cancer, is that process biologically plausible to you?
A No.
Q Not the slightest bit?
A No.
Q Why do you say that?

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A Because, as I -- based on my experience and my reviewing of the literatures up to this point, talc induces a specific type of chronic inflammation that we're terming foreign-body granulomatous inflammation.
I have never seen that, in all my experience in ovarian cancer, foreign-body giant cell reaction. So, I mean, I've seen chronic inflammation in ovarian cancer. No one would dispute that. But specifically the kind of granuloma -- the kind of inflammation induced by talc, I have not observed.
Q Do you know whether you've treated patients or performed surgical pathology on patient specimens of women who used talcum powder for feminine hygiene long-term?
A I wouldn't know if they haven't used it, but I haven't seen any evidence of it when I looked at tissue specimens.
Q So if you're looking at --
MS. AHERN: David, when you get to a stopping point, can we take a potty break.
MR. DEARING: Sure. Let me just wrap up this.
MS. AHERN: Sure.
BY MR. DEARING:
Q So what you're saying is you don't believe that it's biologically plausible that talc can cause

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chronic inflammation that can cause ovarian cancer because you've never seen it; right?
MS. AHERN: Objection. Form.
THE WITNESS: We need to specifically say again the kind of inflammation I'm talking about is foreign-body giant cell inflammation, which is the type of inflammation that's implicated with talc exposure. Talc doesn't produce other types of chronic inflammation.
BY MR. DEARING:
Q Again, you said you've never seen, in your career, a chronic inflammatory response to talc like giant cell granulomas in gynecologic tissue; is that what you are saying?
A That's correct.
Q So my question is, you're saying it's not biologically plausible because you've never seen it; right?
MS. AHERN: Objection. Form.
THE WITNESS: Is that your question?
I've spent, as I said, 40 years looking at gynecologic pathology specimens, including a large number of ovarian cancers, and I have never seen a foreign body -- I've seen a foreign-body giant cell reaction in rare ovarian tumors, endometrial

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carcinomas, due to extrusion of keratin, which can produce a foreign-body giant cell reaction. That, I've seen.
I've seen teratomas, nothing to do with the litigation we're talking about now. It's a completely different kind of tumor. It's a germ cell tumor. And I've seen, with extrusion of keratin in those instances, a foreign-body giant cell reaction.
Apart from those instances and maybe suture granulomas, which, again, are pretty obvious, I haven't seen that type of reaction in association with ovarian cancer during my entire career.
BY MR. DEARING:
Q And are you saying you haven't seen that type of inflammatory reaction in gynecologic tissue to any foreign particle?
A Well --
MS. AHERN: Objection. Form.
THE WITNESS: -- as I just said --
BY MR. DEARING:
Q Except for sutures?
A Suture granulomas and the keratin that I mentioned, which is --
Q That's endogenous?
A Yeah, but it -- yeah, okay. Aside from that,

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I can't recall seeing anything, no.
Q So aside from surgical sutures --
A Uh-huh.
Q -- you've never seen a giant cell granulomatous foreign-body reaction in gynecologic tissue?
A Again, I mentioned the keratin --
Q I'm sorry. Responding to foreign material?
MS. AHERN: Objection. Form.
THE WITNESS: That's correct.
MR. DEARING: Want to take a break?
MS. AHERN: Thank you.
VIDEO OPERATOR BROWN: The time is now 10:31. Going off the record.
(Recess taken.)
VIDEO OPERATOR BROWN: Time is now 10:53. Back on the record.
BY MR. DEARING:
Q Right before the break, Doctor, you made a statement to the effect of "Talc doesn't produce other types of chronic inflammation that can cause cancer." Did you say something like that?
A That's -- that's what I said.
Q So what other types of inflammation do cause cancer that you're referring to?

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A Well, again, in the ovary, there's absolutely no evidence that inflammation causes cancer. I want to be clear about that. Now, there may be other tumors where it plays a role, but those are not things that I'm familiar with.
Q So are you saying that it's not biologically plausible that other types of inflammation can cause ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: I said I haven't observed it and I wasn't aware of anything in the literature that showed chronic inflammation causing ovarian cancer.
BY MR. DEARING:
Q So because you haven't observed it, is it your opinion that it's not biologically plausible?
MS. AHERN: Objection. Form. Misstates his testimony.
THE WITNESS: Well, as I said, I haven't seen it nor have I read any paper that has indicated that it was a causative factor of ovarian cancer.
BY MR. DEARING:
Q And the question is, is it biologically plausible?
MS. AHERN: Objection. Form.
THE WITNESS: Insofar as what the literature has

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described about the type of inflammation induced by talc, which has never shown any evidence of causing cancer, I would say it's not plausible.
BY MR. DEARING:
Q And the type of inflammation caused by talc that you're referring to is talc typically left inside the body from a contaminated surgical tool, for example, surgical gloves maybe back in the day when they still had talc; right?
A Yeah.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q So you're not suggesting that cosmetic-grade baby powder talc is the type of talc that you're referring to that you've seen these other inflammatory responses to; right?
MS. AHERN: Objection. Form.
THE WITNESS: Please repeat -- rephrase that question.
MR. DEARING: Sure.
BY MR. DEARING:
Q You said you expect the inflammatory response to talc to be giant cell granulomatous foreign-body response; right?
A Yes.

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Q And when I -- so my question is, the talc that you're referring to that elicits that type of response is talc left behind from either a surgical tool or a surgical glove or something like that; right?
MS. AHERN: Objection. Form.
THE WITNESS: That's correct.
BY MR. DEARING:
Q And do you agree that the talc used industrially for surgical gloves back in the '70s and before, and potentially contaminating a surgical tool, is different than cosmetic talc in baby powder?
MS. AHERN: Objection. Form.
THE WITNESS: I'm not exactly sure of that. This is something that I don't have expertise in. I would defer to a mineralogist to describe the references between what you describe as industrial and cosmetic talc.
BY MR. DEARING:
Q Just to close the circle, is it your opinion that it's not biologically plausible that any type of chronic inflammation can cause ovarian cancer?
A As I said, I've seen no evidence of chronic inflammation causing ovarian cancer.
Q My question is, is it biologically plausible, in your opinion, that some type of inflammation can

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cause ovarian cancer?
A Well, as I haven't seen it --
MS. AHERN: Objection. Form.
THE WITNESS: -- and I haven't read about it, I -- and it's been studied, I would say it's not biologically plausible.
BY MR. DEARING:
Q What methodology do you use to reach conclusions about biologic plausibility?
A Well, to begin with, as I said early on in the deposition, I have spent 40 years looking at gynecologic pathology, which ovarian cancer is one of those. I have read extensively and kept up with the literature. I've edited the third, fourth, fifth, sixth, and in the process of the seventh edition, of Blaustein's pathology textbook.
I was the lead author on the 2014 WHO classification of ovarian cancer.
I participate in meetings, both domestically and internationally. I review papers, as we discussed earlier.
So I think all of that together amounts to the way I evaluate biological plausibility.
Q Is that a complete description of your methodology used to evaluate biologic plausibility?

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A Well, as I mentioned also, in this particular case, I reviewed what Dr. Kane claimed or alleged that were causative agents. I review those papers specifically. So that in addition to everything else I described.
Q So your methodology for evaluating biologic plausibility is your reliance on your experience, your review of the literature, your publication literature, I guess, and your review of other expert opinions on it?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Did I leave anything out?
A I think that pretty much covers it.
Q And, of course, you haven't published on talc and ovarian cancer?
A That's correct.
Q And you think that's a complete, sound, reliable methodology for assessing plausible -- biologic plausibility?
A Please repeat the question.
Q Sure.
Do you think that that is a complete and reliable methodology for assessing plausible -- biologic plausibility?

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A I believe it is, yes.
Q On page 13 of your report -- and I don't know if you need to look this up. You use the word "inert." You suggest that talc is inert.
I just want to know, what does "inert" mean to you?
A Well, I relied upon -- and I think IARC used that exact same terminology, in fact. And I think in contrast to an inflammatory agent, for example, which elicits more of a systemic immune response, talc is very localized and it induces the migration of macrophages, which then become histiocytes in tissue which surround it and engulf it but don't elicit an immune kind of response. So, in that respect, I think it is, quote/unquote, inert.
Q What do you mean by "immune kind of response"?
A Well, where -- antigen-presenting cells, lymphocytes. Lymphocytes induce various types of reactions in response to an infectious agent, for example. That's not -- that doesn't occur with talc.
Q So you told me why you think talc is inert, but what does it mean to be inert? How do you define "inert," just the word?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I can't do any better than I have.
BY MR. DEARING:
Q Okay. Do you agree that inert particles can cause an inflammatory response that could trigger or be a precursor to cancer?
MS. AHERN: Objection. Form.
THE WITNESS: As I just said, again, I think we specifically -- in this litigation referring to talc as an inert substance that does not produce an inflammatory reaction that can cause ovarian cancer.
BY MR. DEARING:
Q I understand that about talc and that's your opinion.
My question is just because a foreign particle is inert doesn't mean that it can't cause a foreign-body inflammatory reaction that could be a precursor lesion to cancer; right?
MS. AHERN: Objection. Form.
THE WITNESS: No, I disagree with that.
BY MR. DEARING:
Q Well, you would agree that talc does elicit an inflammatory response in tissue; right?
A A specific type of inflammatory reaction, we described foreign-body giant cell granulomatous reaction, yes.

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Q And so if a large talc particle in the peritoneal cavity elicits an inflammatory giant cell granulomatous response and that inflammation is chronic, can't that chronic inflammatory response evolve into a lesion or a precursor lesion for cancer?
MS. AHERN: Objection. Form. Assumes facts.
THE WITNESS: Could you break that? It was a complex question.
BY MR. DEARING:
Q It was a slow question, but it's a simple question.
A Okay.
Q If a large talc particle is left in the peritoneal cavity and evokes the type of response that you say it should, a inflammatory giant cell granulomatous foreign-body response, and it becomes a chronic condition, can't that be a precursor lesion to cancer, some kind of peritoneal cancer?
MS. AHERN: Objection.
THE WITNESS: I don't believe that's true. It's been demonstrated, as you've alluded to before, surgical gloves can introduce talc into the peritoneal cavity. And I'm not aware of any cancer that's been associated or induced by that contamination of talc in the peritoneal cavity.

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BY MR. DEARING:
Q Do you agree with me that inert particles can evoke a chronic inflammatory response, foreign-body response, in the body?
A As I said, inert particles induce a foreign-body giant cell reaction of the sort -- similar to what talc does.
Q Do you agree that talc causes inflammation in epithelial ovarian cells?
A No.
MS. AHERN: Objection. Form.
THE WITNESS: I don't.
BY MR. DEARING:
Q Do you believe that talc can cause inflammation in any kind of ovarian cells?
A Talc produce -- what kind of ovarian cell are we talking about, for starters?
Q Well, any kind you want to identify. Any kind -- let me ask it again.
Do you have any opinions about whether exposure to talc could cause any type of reaction in any type of ovarian cells?
A I've never seen any evidence of that or read any evidence of that.
Q Does that mean you don't think that's

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biologically plausible because you have never seen it?
MS. AHERN: Objection. Form.
THE WITNESS: Let me -- when you're talking about -- you know, the ovary is a complex organ. Contains germ cells, contains stromal cells, contains surface epithelial cells.
Which cells are you actually talking about?
BY MR. DEARING:
Q I'm talking about any type of ovarian cell. I'm leaving it up to you to use any cell you like. Are you telling me that talc causes no reaction in any type of ovarian cell that you know of?
A Well, there have been in vitro studies which have used ovarian cells and shown some reaction, if that's what you mean. I've seen that.
Q Have you seen any studies that suggest that epithelial cells exposed to talc undergo neoplastic changes?
MS. AHERN: Objection. Form.
THE WITNESS: I think it is important to point out, before we get all hung up on ovarian epithelial cells, that if we are talking about -- which, basically, we're talking about causation -- is that ovarian cancer does not start from ovarian epithelial cells; it starts from fallopian tube cells.

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So the fact that it might show some reaction in epithelial cells of the ovary, which some biologic studies -- in vitro studies have shown, doesn't have anything to do with causation of ovarian cancer.
BY MR. DEARING:
Q I realize that's your opinion and you've published that, even. But you agree with me that not all gynecologic pathologists agree with you that invasive ovarian carcinomas start in the fallopian tube?
MS. AHERN: Objection. Form.
THE WITNESS: Could you define which kind of carcinomas you're talking about?
BY MR. DEARING:
Q Sure. Let's start with serous invasive carcinomas. You believe that's those typically start in the fallopian tubes; right?
A Low-grade or high-grade?
Q High-grade.
A High-grade, I believe, start in the fallopian tube.
Q And you would agree with not all gynecologic pathologists degree with you on that; right?
A The consensus at this point in time, 2019, is that a vast, vast majority of pathologists believe that

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ovarian -- high-grade serous carcinoma begins in fallopian tube epithelium.
Q Vast, vast majority of them believe that? Is that what you are saying?
A Well, including your plaintiffs' expert, Susan Kane -- Sarah Kane.
Q I understand.
We'll come back to that.
Is it your testimony that it's not biologically plausible that talc could cause any type of inflammatory reaction in any type of ovarian cell?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I've said, there are some in vitro studies in which exposure to talc has resulted in some proliferation and -- excuse me. I take that back, proliferation -- expression of some markers that are markers of inflammation. Those studies I won't get into it because I'm not, as I said, a bench scientist.
BY MR. DEARING:
Q So there is some evidence that some ovarian cells will respond in an inflammatory way to talc exposure?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Is that what you are saying? There are

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studies.
A That's what I said just now.
Q Okay. Just making sure I understand.
Do you agree that asbestos is a known human carcinogen?
A Yes, I --
MS. AHERN: Objection. Form.
THE WITNESS: Yes, I agree that asbestos is a known carcinogen.
BY MR. DEARING:
Q And you're familiar with IARC, right, the International Agency for Research on Cancer?
A I -- well, I am, yes.
Q And it's an international intergovernmental agency created in 1965; right?
MS. AHERN: Objection. Form.
THE WITNESS: I don't know when it was created, but I'm familiar with IARC.
BY MR. DEARING:
Q And it forms part of the World Health Organization, which is part of the United Nations; right?
A It's part of the World Health Organization.
Q And there are 25 member nations, and it's made up of probably a thousand or more scientists.

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Would you agree with that?
A You'd have to show me the data for that. I don't know.
Q Okay. Well, would you agree it's made up of at least hundreds of scientists?
MS. AHERN: Objection. Form.
THE WITNESS: I want to see what you're talking about. I don't know how many are involved.
(The document referenced below was marked Deposition Exhibit 3 for identification and is appended hereto.)
BY MR. DEARING:
Q I'm handing you Exhibit 3, which is taken from the IARC website, and it identifies IARC's mission statement.
Have you ever seen that before?
MS. AHERN: Objection to the document. Does it have a date?
MR. DEARING: Well, I printed it off yesterday, but no.
MS. AHERN: Okay.
BY MR. DEARING:
Q Have you ever looked at IARC's mission statement before?
A I can't -- hmm. I got twisted up here for a second.
I have -- no, I can't say that I have looked at their mission statement.
Q Okay. Well, in the second paragraph, it says:
"The objective of the IARC is to promote international collaboration in cancer research. The agency is interdisciplinary, bringing together skills in epidemiology, laboratory sciences, and biostatistics to identify the causes of cancer so that preventative -- preventive measures may be adopted and the burden of disease and associated suffering reduced. A significant feature of the IARC is its expertise in coordinating research across countries and organizations. Its independent role as an international organization facilitates this activity. The agency has a particular interest in conducting research in low- and middle-income countries through partnerships and collaborations with researchers in these regions."
Is that your understanding of IARC's mission?

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A Well --
MS. AHERN: Objection. Form.
THE WITNESS: -- that's what it states.
BY MR. DEARING:
Q Do you have any --
A I have no reason --
Q -- that that's not --
A -- to argue with it.
Q Okay. Are you aware that in 2009 IARC issued a monograph that stated that there is sufficient evidence now available to show that asbestos causes cancer of the ovary?
A I am aware of it. I would question their methodology and who the individuals were on that committee that came to that conclusion, because, in looking at that, and I am familiar with it, I had significant issues with the -- their methodology that they used and the conclusions that they drew from that.
Q Do you believe asbestos can cause ovarian cancer?
A At this point, I do not believe that's the case.
Q That same monograph states that "Studies suggest that asbestos can accumulate in the ovaries of women who are exposed to it."

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Do you agree with that statement?
MS. AHERN: Objection. Form.
THE WITNESS: The -- as I recall, those studies that they're citing were inhalation studies of very -- of occupational -- of people that were exposed occupationally or environmentally to very high doses of asbestos and which bear -- nothing to do with perineal exposure.
BY MR. DEARING:
Q The question is do you agree that studies suggest that asbestos can accumulate in the ovaries of women who are exposed to it?
A I'd have to see the studies where it shows that.
Q So you don't have an opinion on that?
A No. I said I'd like to see the studies. I don't believe -- I'd like to see it.
Q I don't have them.
A Okay.
Q So I'm asking do you have an opinion on that.
A My opinion is, as I said earlier, asbestos does not cause ovarian cancer.
(The document referenced below was marked Deposition Exhibit 4 for identification and is appended hereto.)

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BY MR. DEARING:
Q This is Exhibit 4, and this is the monograph I'm referring to.
If you look at -- have you seen this before, this monograph? This is where those statements came from.
A I have seen the monograph, I don't specifically recall this page.
Q Okay. Well, look at the bottom of it, that table. And do you see -- these are Group 1 agents, and IARC defines Group 1 agents as known human carcinogens; right?
A Yes, correct.
Q And it identifies, first of all, arsenic as a known human carcinogen, and it identifies tumor sites for which there is sufficient evidence of human carcinogenicity as lungs, skin, urinary bladder.
Do you see that?
A In the second column I see lungs, skin, yes, urinary bladder. Uh-huh.
Q And a little bit further down it identifies chromium as a Group 1 carcinogenic.
Do you see that?
A I do.
Q And it identifies the lung as a potential

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tumor site for chromium cancer; right?
A Yes.
Q And then right below that is nickel, nickel compounds, is identified as a Group 1 agent. And it identifies tumor sites for which there is sufficient evidence in humans as lungs, nasal cavity, and paranasal sinuses.
Do you agree?
A I see that.
Q Do you agree that arsenic, chromium, and nickel are known human carcinogens?
A Well, according to IARC, they are.
Q Do you agree that they are?
A I agree with IARC on that.
Q And then right below that, another Group 1 agent, it says asbestos. And then it identifies -- one, two, three, four -- six types of asbestos. And it states the tumor sites for which there is sufficient evidence in humans are lung, mesothelioma, larynx, and ovary.
And are you saying now that you disagree that the ovary -- that this is sufficient evidence that asbestos can cause cancer in the ovaries?
A I agree that the -- I agree with what I said earlier, that the evidence upon which IARC came to the

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conclusion about ovarian cancer has significant issues that I would argue with.
Q That's not my question. My question is do you agree that asbestos can cause cancer in the ovary, like IARC says?
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: I just said I don't agree that it causes ovarian cancer.
BY MR. DEARING:
Q Do you -- if you move over to the fourth column under asbestos, it describes the established mechanistic events that cause the cancer. And it says the asbestos causes "impaired fiber clearance leading to macrophage activation, inflammation, generation of reactive oxygen and nitrogen species, tissue injury, genotoxicity, aneuploidy and polyploidy epigenetic alteration, activation of signaling pathways, resistances to apoptosis."
So do you agree asbestos can cause lung cancer?
A Yes.
Q Do you agree that that's the mechanism by which asbestos can cause lung cancer?
MS. AHERN: Objection.
THE WITNESS: I should clarify what I just said a

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moment ago using the term "cancer." And what I would say is that asbestos is primary -- causes mesotheliomas, which is a type of cancer but is very different from adenocarcinoma or squamous cell carcinoma of the lung, and which asbestos is -- plays maybe a contributory role, but certainly not the major role.
BY MR. DEARING:
Q Okay. So my question is do you believe that asbestos can cause mesothelioma or other lung cancers by the mechanism that's described in this table?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I'm not an expert on mesothelioma and asbestosis. However, I would agree that asbestos causes mesothelioma -- pleural mesothelioma and potentially these mechanisms might explain it, but I haven't studied it.
BY MR. DEARING:
Q So you say that might be the mechanism, but you just don't know?
A Well, I haven't studied it. I don't specialize in asbestosis.
Q I'm not faulting you. I'm just saying you're saying that could be, but you don't know. Does that mean you don't have a concrete opinion on that, whether

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that's the mechanism that causes mesothelioma?
A Well, these are the mechanisms that IARC describes which, you know, may be reasonable. But, again, I don't have direct personal experience with that. So I can't confirm every one of these features.
Q Okay. It also suggests that asbestos causes cancer in the larynx.
Do you agree that -- that that's true?
MS. AHERN: Objection. Form.
THE WITNESS: I really don't know about the laryngeal carcinoma.
BY MR. DEARING:
Q It also says there are possibly other sites where asbestos causes cancer -- the colorectum, the pharynx, the stomach.
Do you have any opinion about whether asbestos causes cancer in those organs?
A Again, these are areas that I'm not -- I have no involvement with. So I can't really comment.
Q Are you aware of other cancers that are caused by this mechanistic process that's described here by IARC for asbestos?
MS. AHERN: Objection. Form.
THE WITNESS: Could you rephrase that question?
MR. DEARING: Sure.

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BY MR. DEARING:
Q Are you aware of other cancers or do you have knowledge to explain whether other cancers may be caused by this mechanistic process described by IARC pertaining to asbestos?
A Again, I mean, with established mechanistic events, things like resistance to apoptosis, activation of signaling pathways, epigenetic alteration, genotoxicity, these are general mechanisms that have been implicated in the development of cancer in general.
Q So looking at this mechanism that's described by IARC, it says, "Impaired fiber clearance leading to macrophage activation."
Do you agree that macrophage activation is a foreign-body response in the body?
MS. AHERN: Objection. Form.
THE WITNESS: Macrophages can be induced by a variety of -- well, of course, you mentioned foreign-body giant cell reaction, but other types of inflammation can also induce the presence of macrophages.
BY MR. DEARING:
Q And giant cell granulomas are an agglomeration of macrophages; right?

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A Well, in the tissue, they're referred to histiocytes, but they're basically macrophages.
Q So a giant cell is a joined group of macrophages; right?
A Correct.
Q So according to this mechanism described by IARC, macrophage activation occurs, which appears to be defined as inflammation.
Would you agree that that's what they mean there by saying "inflammation"?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said just a moment ago, macrophage activation can occur with a variety of inflammatory reactions, not just only foreign-body giant cell.
BY MR. DEARING:
Q Okay. Macrophage activation is a type of inflammation; right? Is that a fair statement?
A Not really. It's part of the inflammatory reaction. There are other cells as well -- lymphocytes, plasma cells, eosinophils, polymorphonuclear leukocytes. Macrophages are one type of cell involved in inflammation.
Q And then do you agree that inflammation can lead to the generation of reactive oxygen and nitrogen

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species?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Is that outside your specialty?
A Again, I mean, I've read enough about that to know that, yes, macrophage activation could induce reactive oxygen species.
Q And reactive nitrogen species.
A And reactive nitrogen species.
Q And can reactive oxygen species and reactive nitrogen species damage DNA?
A Can it damage DNA? Yes.
Q And damaging, DNA, of course, can cause uncontrolled proliferation of cells; correct?
MS. AHERN: Objection. Form.
THE WITNESS: Well --
BY MR. DEARING:
Q I know there's some steps in between, but I'm trying to speed this up.
MS. AHERN: Same objection.
THE WITNESS: Well, involvement -- interjection of a certain agent into DNA can cause DNA damage, that's true.
BY MR. DEARING:
Q I'm not talking about certain agents. I'm

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talking specifically about reactive oxygen species and reactive nitrogen species. Those agents can damage DNA; right?
A Yes, they can.
Q And then cells with damaged DNA can become cancer cells, can't they?
MS. AHERN: Objection. Form.
THE WITNESS: Not necessarily. Not all of them do. Some might.
BY MR. DEARING:
Q Well, would you agree that all cancers are borne out of some genetic disruption?
MS. AHERN: Objection. Form.
THE WITNESS: The issue is it plays a role in carcinogenesis. But DNA damage, in and of itself, does not invariably lead to malignant transformation.
BY MR. DEARING:
Q Right. But I'm asking the inverse of that question.
You can't have cancer without original DNA damage; right?
A That's --
MS. AHERN: Objection. Form.
THE WITNESS: DNA damage is part of the process of development of a carcinoma.

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BY MR. DEARING:
Q So thank goodness you can have DNA damage without cancer, but you can't have cancer without DNA damage; right?
MS. AHERN: Objection. Form.
THE WITNESS: As far as I know, all cancers are part of -- part of the development of cancer is dependent on damage -- or I should say genotoxicity, which means damage in DNA in some form.
BY MR. DEARING:
Q And resistance to apoptosis can also be a result of DNA damage; right? That's part of the problem with cancer is the cells don't -- they lose their programmed ability to self-destruct; right?
MS. AHERN: Objection. Form.
THE WITNESS: That's one of the factors in carcinogenesis, one of the factors.
BY MR. DEARING:
Q But that resistance to apoptosis is a result of DNA damage; right?
MS. AHERN: Objection. Form.
THE WITNESS: Generally speaking, it's an activation of a suppressor gene called p53, maybe some other genes as well.
///

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BY MR. DEARING:
Q So as I mentioned, this is from 2009; right? Do you agree with me?
A I think that's --
Q The date is at the very bottom of the page.
A Yeah.
Q It's right under the table, actually.
A I see it, 2009.
Q Okay. So in 2009 IARC said, "Epidemiological evidence has increasingly shown an association" --
A Where are we reading now?
Q I'm sorry. The top of page 454, so the other page, very top.
A Uh-huh.
Q "Epidemiological evidence has increasingly shown an association for all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite, and anthophyllite) with an increased risk of lung cancer and mesothelioma."
Do you agree with that statement?
A Yes.
Q It goes on to say:
"Although the potency differences

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with respect to lung cancer or mesothelioma for fibers of various types and dimensions are debated, the fundamental conclusion is that all forms of asbestos are carcinogenic to humans."
Do you agree with that?
MS. AHERN: Objection. Form.
THE WITNESS: Well, again, I'm not an expert on the different types of asbestos. I would leave -- I would defer that to an mineralogist to agree as to whether all types, as they state here, are associated with cancer.
BY MR. DEARING:
Q The next sentence says:
"Mineral substances, for example, talc and vermiculite, that contain asbestos should also be regarded as carcinogenic to humans."
Do you agree with that statement?
A Well, that's --
MS. AHERN: Objection. Form.
THE WITNESS: That's what IARC states. Again, I don't agree with that, but that -- they state that, but I don't agree with it.
///

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BY MR. DEARING:
Q If a mineral substance contains carcinogenic asbestos, doesn't that make that mineral substance carcinogenic?
MS. AHERN: Objection. Form.
THE WITNESS: We have no idea how much asbestos is in there. It might be a totally minute amount, that there's a contaminant that doesn't have any relationship to the development of cancer.
BY MR. DEARING:
Q Well, you would agree with me that the FDA has determined that there's no safe level of asbestos exposure; right?
MS. AHERN: Objection. Form.
THE WITNESS: As I said earlier, when it comes to the specifics of the composition of asbestos or, for that matter, talc, I would defer to a mineralogist.
BY MR. DEARING:
Q Then the next sentence is what I read to you already:
"Sufficient evidence is now available in 2009 to show that asbestos also causes cancer of the larynx and of the ovary."
And you disagree with that statement, even as

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it applies in 2019?
A Well, if you read further down the paragraph, you'll see that it says -- let's see, one, two, three, four, five, six, seven, eight -- ten lines, it says:
"Cohort studies of women who were heavily exposed to asbestos in the workplace consistently report increased risks of ovarian cancer, as in a study of women in the UK who manufactured gas masks during World War II."
Q Right.
A "Studies suggest asbestos can accumulate in the ovaries of women who were exposed to it."
So you're talking about massive exposures of asbestos in women who are occupationally exposed. The numbers of cases, I looked at that, are very small because most of people who worked in that industry were men.
So, again, you're referring to small numbers of cases, extremely heavy exposure to asbestos that allows them to come to that conclusion, which is what I dispute.
Furthermore, I think there's a significant risk that cases called ovarian cancer -- you'll notice that there's no pathologist in the -- in the group in

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this -- in that statement that we read earlier, no pathologist in the IARC group. And I would dispute the fact that these are all carcinomas of the ovary. They may be mesotheliomas that were misclassified.
Q Okay. Do you believe asbestos can cause mesothelioma of the ovary?
A Well, I'd have --
MS. AHERN: Objection. Form.
THE WITNESS: I'd have to, again, review the data. I can tell you I hardly ever see, and there were hardly any reports of, mesotheliomas involving the ovary.
BY MR. DEARING:
Q The last sentence you just read, "Studies suggest that asbestos can accumulate in the ovaries of women who are exposed to it," do you agree or disagree with that?
A Well, let's look at the reference that they're talking about.
Q It's the Heller study.
A Heller study.
Q Drs. Heller, Gordon, Westhoff, Gerber.
A Yeah, maybe we could look at that and see what they say.
Q Okay. Well, you know, in that study, they -- they used transmission electron microscopy to digest

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tissue to measure the burden count of asbestos fibers in the tissue.
Do you know that about that study?
MS. AHERN: Objection. Form.
THE WITNESS: I'd like to see the study.
BY MR. DEARING:
Q Okay. So you have no opinion about that right not without seeing the study that --
A Well, it's been a long time --
Q Let me finish the question, please.
A Yeah, sorry.
Q So you have no opinion about whether asbestos can accumulate in the ovaries of women who are exposed to it?
A I said I'd like to see the study.
Q That doesn't answer my question. You either have an opinion or you don't.
MS. AHERN: Objection. Form.
THE WITNESS: My answer is I can't come to an opinion until I've seen the study.
BY MR. DEARING:
Q Okay. And you don't know whether you've seen the study before?
A I have seen the study, but I'd like to see it again. It's been a while.

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Q Okay. All right. Do you have any opinion about whether Johnson & Johnson baby powder or Shower to Shower product has any form of asbestos in it?
A I'll repeat what I said earlier that I'm just talking about the talc that I read. I don't know what's in their -- what's in their bottles of baby powder or Shower -- whatever. I would depend on -- I would depend really -- because it's complex. It's complex. It's debated. There are subtle differences between how much, what the type of asbestos is.
So I would really have to defer to a mineralogist to answer that question.
Q Are you familiar with the term "asbestiform fibrous talc"?
MS. AHERN: Objection. Form.
THE WITNESS: I've heard it mentioned.
BY MR. DEARING:
Q Do you feel like you know enough about it to discuss it?
A No.
Q Based on what you've read -- and maybe you haven't read anything about this -- do you have an opinion about whether Johnson & Johnson's baby powder or Shower to Shower products have asbestiform fibrous talc in them?

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MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: I'll just repeat what I said before. All I'm referring to is what they say talc is in the various studies. I don't know all the details of the composition of the talcum powder that they use.
BY MR. DEARING:
Q Since you have an opinion that talc cannot cause any type of inflammatory reaction that could cause ovarian cancer, don't you think it's important to know something about whether that talc is platy talc or asbestiform fibrous talc, or what type of talc it is?
A No. It doesn't matter. Whatever it is hasn't been shown to form ovarian cancer.
Q Is it your opinion that asbestos exposed to ovaries doesn't cause cancer either?
A I'm not convinced of it at this point. I'd like to see more studies.
Q Okay. Is it biologically plausible that asbestos could cause ovarian cancer?
A Biologically plausible? Again, to me, it's -- it has to be seen. And I haven't seen that yet. I'd like to see more studies, and then I could tell you whether I think it's biologically plausible or not.
Q So you don't know whether it's biologically plausible, as you sit here right now?

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A I'm saying I'd like to see more studies to be more convinced that it might be biologically plausible. At this point, I'm not convinced.
Q That doesn't answer my question. I know you would like to see more studies.
My question is, do you have an opinion one way or the other whether asbestos exposure to ovaries -- do you have an opinion one way or the other whether it's biologically plausible that asbestos can cause ovarian cancer? Just do you have an opinion?
If you don't have an opinion, that's fine. I just want to know.
A When I repeat it --
MS. AHERN: Objection. Form.
THE WITNESS: -- I'm repeating what I said earlier.
BY MR. DEARING:
Q I know you want to see studies.
Does that mean you don't have an opinion?
A At this point, I'm not convinced that it's biologically plausible to cause ovarian cancer. I want to see something that shows me evidence of that, and I don't see it.
Q Well, what would you want to see that would show you evidence that it's biologically plausible that ovarian -- that asbestos exposure can cause ovarian

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cancer?
A It would be nice to see asbestos in ovaries causing a fibrous reaction, maybe seeing some ferruginous bodies, which are very characteristic of asbestos exposure in patients who have ovarian cancer.
Q And while we're talking about this, what would you expect to see or want to see regarding biologic plausibility of talc causing ovarian cancer?
A Well, we kind of --
Q Same thing?
A -- discussed that earlier that with -- I'd like to see a chronic foreign-body giant cell granulomatous reaction, something to indicate that it's biologically active and not just sitting there, say, as a contaminant.
Q Okay. That's all you would want to see?
A I'd like to see ovarian cancer associated with it, an ovarian cancer in which these -- this is associated with what I just described.
Q How would you make the connection between a foreign-body response to talc in the ovary and cancer of the ovary? If you saw the foreign-body reaction that you're saying you want to see, is that enough to say, "Well, if that's there, it may be able to cause cancer"?

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A Not at all.
MS. AHERN: Objection. Form.
THE WITNESS: No, not at all.
MR. DEARING: Okay.
THE WITNESS: And I'll give you a specific example of something -- where that kind of information was very misleading.
I was involved, and I have been involved for the last 15 years, with HPV and cervical --
BY MR. DEARING:
Q Excuse me, Doctor. I don't mean to cut you off. I know about HPV virus. I don't need to talk about that.
MS. AHERN: Let him answer, and then you can object as nonresponsive.
MR. DEARING: Well, he's clearly not, and I have a limited amount of time.
BY MR. DEARING:
Q What I'm saying is, what do you say about talc?
A I'm going to talk about why seeing the presence of a substance in the ovary with the cancer doesn't mean that it's causing the cancer.
And I was -- before you interrupted me, I was going to say that, in the 1960s, '70s, and '80s, HSV-2,

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herpes simplex virus type 2, was thought to cause cervical cancer. There were electron micrographs showing HSV-2 particles in cervical cancer.
There were zero epidemiologic studies confirming that HSV caused cervical cancer with relative risks like ten, much higher than you see with talc, and it was all wrong. As you said, it's -- you know HPV causes it, not herpes.
So just the presence of that in the ovarian tumor doesn't mean that it causes cancer.
MR. DEARING: Right. I move to strike as nonresponsive.
BY MR. DEARING:
Q My question is, what do you need to see between the foreign-body response that you're describing and the cancer to link the two? That's the question.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q What do you need to see?
MS. AHERN: Objection. Form.
THE WITNESS: I'd like to see fulfillment of the various criteria that we've talked about before, Bradford Hill, to really say that all the various studies, not just biologic plausibility but strength of

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association from epidemiologic studies, dose response, consistency, the various factors that Bradford Hill requires to show causality. That's what I want to see, and I haven't seen that.
BY MR. DEARING:
Q So there's nothing pathologically you want to see?
A Well, that might explain --
MS. AHERN: Objection. Form.
THE WITNESS: That may be one factor that could be considered.
BY MR. DEARING:
Q So back to my question.
What pathologically you would expect to see in tissue such that you would link the formation of foreign-body response to the cancer?
MS. AHERN: Objection. Form.
THE WITNESS: I would like to -- I haven't ever seen it. Okay. So I don't know what I would expect. It's a completely hypothetical question. I'd have to see what I see, and then I could tell you an answer.
BY MR. DEARING:
Q Are you aware that IARC also classified asbestiform talc fibers as carcinogenic?
A Are you distinguishing that from just other

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types of asbestos?
Q Asbestiform talc fibers are not asbestos.
A I'm sorry. Repeat your question.
Q Yes. I am distinguishing those two. And if you don't know this and I'm outside of your wheelhouse, just tell me and I'll move on.
A Yeah.
Q Asbestiform talc fibers --
A Oh, okay.
Q -- so not asbestos.
Are you aware that IARC has identified asbestiform talc fibers as carcinogenic to humans?
MS. AHERN: Objection. Form.
THE WITNESS: I'm not aware of that.
MR. DEARING: Would that fact affect your opinion about whether talc can cause ovarian cancers?
THE WITNESS: No.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Have you read the 2012 IARC Monograph?
A You'd have to show it to me. I don't recall.
Q Well, it's on your reference list.
A Yeah. Well, I'd have to see it again.
Q Okay.
///

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(The document referenced below was marked Deposition Exhibit 5 for identification and is appended hereto.)
BY MR. DEARING:
Q Doctor, I'm marking as Exhibit 5 a portion of the 2012 Monograph, and the reason is it's several hundred pages long and I'm trying to save some trees.
But here is the portion that I want to talk to you about. First of all --
MS. AHERN: I'm sorry, one second. Could I get a copy? Thank you.
BY MR. DEARING:
Q So obviously the cover there identifies this as an IARC Monograph, and it's addressing arsenic, metals, fibers, and dust. And it's Volume 100C.
Do you see that?
A Yes.
Q And this is the one that you referenced in your reference list; right?
A Yes.
Q And you think you have seen this before? You've read this?
A Yes.
Q If you would, turn to page 230.
Do you see the section entitled "Talc

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Containing Asbestiform Fibres"?
A Where am I? 230?
Q I think you're on 231.
A Oh, yeah.
Q It says:
"Talc particles are normally plate-like. These particles, when viewed on edge under the microscope, in bulk samples or on air filters, may appear to be fibers and have been misidentified as such. Talc may also form true mineral fibers that are asbestiform in habit. In some talc deposits, tremolite, anthophyllite, and actinolite may occur. Talc containing asbestiform fibers is a term that has been used inconsistently in the literature. In some contexts, it applies to talc containing asbestiform fibers of talc."
Do you feel like you have an understanding of asbestiform talc fibers based on that explanation of what they are to talk more about them, or are we still outside of your expertise?
A I like the term where it says "inconsistently

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in the literature."
Q Right.
A So if it's inconsistently in the literature, I, as not a mineralogist, would have a lot of trouble dissecting all that out.
Q It's inconsistent in the literature because some authors treat asbestiform talc as asbestos, and there's some confusion in the name. They should have named it something else, but that's the confusion they're talking about.
MS. AHERN: Objection to the characterization.
BY MR. DEARING:
Q Anyway, we'll move on to the human exposure section, page 232. The subheading is "Human Exposure."
A Yes.
Q And it says -- and this explains -- this is the way IARC explains exposures and explains carcinogenesis of the identified carcinogens is they first talk about how humans get exposed to it.
And they say here that:
"Consumer products (cosmetics, pharmaceuticals) are the primary source of exposure to talc for the general population. Inhalation and dermal contact, (i.e. through perineal

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application of talcum powders) are the primary routes of exposure."

Do you agree with that statement that inhalation and dermal contact, such as through perineal application of talcum powders, is the primary route of exposure for talc for humans?

MS. AHERN: Objection. Form.

THE WITNESS: As far as I know, inhalation and perineal exposure are the main contacts.

BY MR. DEARING:

Q Right. In -- when they describe that exposure, IARC is describing exposure to the general population; right? That's what it says right above it --

A Yeah.

Q -- "exposure to the general population"?

A That's what it says.

Q Okay. That's all I'm going to ask you about that.

Do you agree with the statement that "Patients with chronic aspirin, nonsteroidal anti-inflammatory drugs, or acetaminophen use have a reduced risk of ovarian -- epithelial ovarian cancer"?

MS. AHERN: Objection.

MR. DEARING: That was terrible. Let me start all

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over. Good grief.

BY MR. DEARING:

Q Do you agree that patients with chronic aspirin, nonsteroidal anti-inflammatory drug, or acetaminophen use have a reduced risk of epithelial ovarian cancer?

A So you're referring to the epidemiology studies, I assume?

Q There are several studies, yes.

A Yeah. Well, from what I recall, and it's been a while, they are inconsistent. Some show that they decrease risk. And some, specifically the NSAIDs, as I remember, did not show there was a reduced risk of ovarian cancer.

Q Do you have an opinion professionally?

A Well --

MS. AHERN: Objection. Form.

THE WITNESS: -- as I said, I'm not an epidemiologist, I'm not going to get into the nitty-gritty of it, but just based on those studies, I would say that it's not -- it's inconsistent.

BY MR. DEARING:

Q Do you believe that talc can migrate from the perineum through a woman's reproductive tract to the ovaries?

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A Absolutely not.

Q What is retrograde menstruation?

A Retrograde menstruation occurs in women when they have, at the time of menses, instead of the breakdown of the lining of the uterus, which is the endometrium, passing through the cervix, the vagina, and going as we normally -- as normally occurs in menstruation, goes the other way and goes through the fallopian tubes to the peritoneal cavity.

Q And you agree that 90 percent of women with healthy fallopian tubes experience retrograde menstruation?

MS. AHERN: Objection. Form.

THE WITNESS: I don't know what the percentage is, but I'm sure it's frequent.

BY MR. DEARING:

Q In your report on page 9, you have a short discussion here about endometriosis and endometrioid carcinomas.

A Let me get there. Okay. Page 9.

Q Right. You say in the third sentence:

"The precise origin of endometriosis has not been conclusively established. Proposed mechanisms include retrograde menstrual flow and in

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situ development in the peritoneum through a process of metaplasia. Other mechanisms, including development of embryonic rests, have also been invoked. Most cases are best accounted for by retrograde menstruation, that's endometrial tissue expelled at the time of menstruation which passes through the fallopian tubes and implants on the ovary or other sites in the peritoneal cavity."

Now, I assume, because you put this in your report, that's what you believe causes endometriosis. Is that right?

MS. AHERN: Objection form.

THE WITNESS: Yes, that's correct.

BY MR. DEARING:

Q But you acknowledge that has not conclusively established; right?

A Generally -- it's generally thought to be the case.

Q Right. But you write, "The precise origin of endometriosis has not been conclusively established." Right?

A True.

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Q Does that mean other gynecologic pathologists disagree with you on that mechanism?
MS. AHERN: Objection to form. Which mechanism?
BY MR. DEARING:
Q Is that what you mean by that?
A Yeah.
Q That endometriosis is caused by this process that you just described.
A In other words, that endometriosis can be caused either by retrograde menstruation, metaplasia, or from embryonic rest. That covers it all.
Q Okay. I want to put a diagram up, just because this makes it easier for me to talk about it. I can hand you one if you prefer, if it is easier to see, but -- I have lots of them.
MS. AHERN: Thank you.
THE WITNESS: Might as well take advantage of your generosity. Okay.
BY MR. DEARING:
Q So now using this diagram to describe this retrograde menstruation that you're talking about.
A Uh-huh.
Q So what you're saying is that the endometrium -- the endometrial tissues expelled during menstruation. Can you show me on your diagram, and

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then I'll repeat it here, where that tissue is coming from that's being expelled?
A Yeah. It's coming from this little -- where it says "uterus."
Q Right.
A It's like a V.
Q Uh-huh.
A That's the lining of the uterine cavity, endometrial tissue.
Q Okay.
A And that's what breaks down and is expelled.
Q So this area that I'm circling -- and I know this is not a three-dimensional diagram, but essentially it's the lining of the uterus that's being expelled; right?
A That's correct.
Q So you are saying during retrograde menstruation, this lining is expelled in the endometrium and then passes through the fallopian tubes, out the fimbriated end of the fallopian tube, to the ovary?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Am I stating that correctly?
A That is -- yes. And other parts of the

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peritoneal cavity as well.
Q When that reverse flow transports that endometrial tissue, does it pick up anything else when it goes?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Anything else that might be in that cavity? Any other cells?
MS. AHERN: Objection. Form.
THE WITNESS: There are no other cells. There's just the endometrium.
BY MR. DEARING:
Q What if there were bacterium in that area? Would the retrograde menstruation pick up the bacterium and deliver them to the ovaries with the tissue?
A Well, certainly, women who have pelvic inflammatory disease, sexually transmitted disease, it involves the fallopian tubes. So somehow or another, the bacteria get there. Now, whether they come by lymphatics, I don't know. It's usually thought to be through lymphatics, not necessarily retrograde menstruation.
Q Okay. My question is, if there were other materials in that tissue that's being transported, whether it's bacteria, whether it's foreign material,

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don't you think -- or don't you agree that it could also be picked up and transported through the fallopian tubes to the ovaries?
MS. AHERN: Objection. Form.
THE WITNESS: It is complete speculation. I have no idea.
BY MR. DEARING:
Q You also state in your report that --
A Back to the report. Specific page?
Q Yes. Well --
A Tell me where we are.
Q I don't remember where I read it, and we can look for it in a minute, but let me just ask you the question.
Do you agree that the epidemiological data indicate a protective effect of tubal ligations against ovarian cancer in general and an even stronger protective effect for endometrioid and clear cell carcinomas, which are sometimes associated with endometriosis?
MS. AHERN: Objection.
THE WITNESS: It reduces the risk of those, specifically endometrioid and clear cell, yes.
BY MR. DEARING:
Q Doesn't the epidemiological data also evidence

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a protective effect of ovarian cancers in general, all histologic types of ovarian cancer, by tubal ligation?
MS. AHERN: Objection. Form.
THE WITNESS: I'm not sure -- there's data for high-grade serous carcinoma. I'm not aware of data for low-grade serous carcinoma. I'm not aware of data on mucinous. I'm not aware of that. But for other -- certainly high-grade serous carcinoma.
BY MR. DEARING:
Q Would you agree that high-grade serous carcinomas make up about 80 percent of the ovarian cancers?
A Yes. But I should add, as I put in my report, that's not the only explanation. You're implying that retrograde menstruation is what -- has reduced the risk of high-grade serous carcinoma. I think there's another statement in there that I made which indicates that tubal ligation has been demonstrated in both humans and animals to reduce or make that epithelium on the fimbriated end of the tube more quiescent, meaning less proliferation, less likelihood of mutations occurring. And perhaps that's another mechanism that reduces the risk of high-grade serous carcinoma.
Q I don't remember seeing that in your report, but you do say, "Also supportive of this" -- and I'm on

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page 9, near the bottom of that paragraph.
"Also supportive of this hypothesis are epidemiologic data that indicate the protective effect for tubal ligation is stronger for endometrioid and clear cell carcinoma than for high-grade serous carcinoma" --
A I'm sorry. Could you just tell me where you are reading again? I want to make sure you're right.
Q Sure. It is middle of that page --
A "This suggests"?
Q -- bottom of the paragraph.
A Is that --
Q Below "this suggests."
A Okay. "This suggests." Okay.
Q "Also supportive" --
A Okay. Got you.
Q "Also supportive of this hypothesis" -- and you're talking about this retrograde menstruation that delivers endometrial tissue the ovary?
A Right.
Q "Also supportive of this hypothesis are epidemiologic data that indicate the protective effect for tubal ligation is stronger for endometrioid and clear cell

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carcinoma than for high-grade serous carcinoma, presumably because tubal ligation interrupts the retrograde passage of endometrial tissue from the uterus to the peritoneal cavity."
A Correct, but you have to keep reading.
Q "However, this mechanism does not fit well with the development of high-grade serous carcinoma, which is now thought to derive from a precursor lesion in the fimbriated end (the most distal portion) of the fallopian tube, which is in close contact with the ovary."
I understand that, and I'm going to talk a lot about --
A Read the next sentence.
Q Okay.
A "Importantly, Tiourin, et al., demonstrated in humans and mouse models 'that tubal ligations induces quiescence of distal fallopian tube epithelium' by decreasing the number and proliferation of progenitor cells in that region, which can explain the slight reduction

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in the risk of high-grade serous carcinoma associated with this procedure."
Q Okay. But you agree with me that epidemiologic data shows a protective effect for high-grade serous carcinoma in particular for women who have undergone tubal ligations?
MS. AHERN: Objection. Form.
THE WITNESS: Yes. Slightly less than it is for endometrioid and clear cell carcinoma.
BY MR. DEARING:
Q And for endometrial -- endometrioid and clear cell carcinomas, it's a significant reduction in risk, isn't it?
A I don't --
Q Tubal ligation.
A Yes, it definitely plays a role.
Q And it makes perfect sense because, if you occlude the tubes, nothing can pass through them; right?
MS. AHERN: Objection.
THE WITNESS: Right.
How we doing with our bladders?
MS. AHERN: Do you need to go?
THE WITNESS: I drank too much coffee.

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MR. DEARING: Want to take a break?
THE WITNESS: Yeah. Would that be okay?
MR. DEARING: Absolutely. Anytime. Please tell me. I get carried away.
VIDEO OPERATOR BROWN: Time is now 11:59. Going off the record.
(Lunch recess taken.)
VIDEO OPERATOR BROWN: Okay. Time is now 1:02. Back on the record.
BY MR. DEARING:
Q Doctor, you mentioned a few minutes ago -- a while ago about your textbook that you edited.
It's called "Blaustein's" --
A -- "Pathology of the Female Genital Tract."
Q And you're the primary editor of that textbook; is that right?
A I was until the last edition. I had two junior people join me, and they're doing that with me on this current edition that we're working on.
Q What is the last edition that was published?
A The sixth edition.
Q And how many editions have you edited?
A Third, fourth, and fifth by myself. Sixth with the two of them, and now the seventh with these two people.

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Q And in addition to editing the textbook, have you also authored chapters within the textbook?
A Yes, I have.
Q And who is the intended audience for that textbook? Is it for medical students? Doctors? What?
A Yes.
Q Anybody that's interested?
A Right. Residents, fellows, gynecologists, pathologists in practice, medical students.
Q It's a pretty well-recognized and accepted authority on gynecologic pathology; isn't it?
A Well, it's one among many.
Q Going back to the retrograde menstruation process we were talking about at the break, what's the biologic mechanism that causes this reverse upstream menstrual flow?
A I don't know that anyone knows.
Q Well, have you ever observed that process taking place?
A Observed it? You mean like with a laparoscope and watched the blood flow? No, I haven't.
Q Have you observed any evidence of that process taking place with the exception of the endometrial tissue being implanted on the ovary?
A Please clarify. Rephrase that question.

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Q Sure.
So you've never actually seen the flow take place, obviously. Have you seen any evidence that that flow takes place that makes you think it exists?
A Well, I've seen in microscopic slides of the fallopian tube taken out at the time a woman is menstruating, seen collections of blood and broken-down endometrium within the tubal lumen.
Q Okay. So retrograde menstruation takes place during a woman's regular menstrual cycle, or is it some other time during that --
A No, during the time of the menstrual cycle.
Q So the menstrual fluid is flowing both ways at the same time?
A Well, conceivably, yes. It's going out in the normal pathway, but also collections of the same kind of material can be seen in the lumen of the fallopian tube. Not often, but we've seen it.
Q Is it your testimony that the only way that those endometrial cells could get to the lumen of the fallopian tube or to the ovaries is by this retrograde menstruation?
MS. AHERN: Objection to form.
THE WITNESS: Yeah. I can't imagine how they would get there any other way.

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BY MR. DEARING:
Q How does -- how do endometrial cells implanted on the surface of the ovary cause endometrioid carcinoma?
A Well, there's some interesting studies showing that, when you look at the endometrium of women with endometriosis -- so I'm saying the endometrium, within the lining of uterus -- and compare that to women who don't have endometriosis, there are certain molecular changes in the women with endometriosis -- in the lining of the uterus, in the endomet- -- that are different than the women who don't have endometriosis, suggesting that there's something different about that endometrium in women with endometriosis that leads to the development of endometriosis compared to other women who may also have retrograde menstruation but who don't develop endometriosis.
Q Right. But what mechanism takes place to turn a displaced endometrial cell on the surface of the ovary in an endometrioid carcinoma?
A Oh. Well, there's certain molecular genetic alterations that occur.
Q Do they occur once they get to the ovary, or do they occur on the way to the ovary, or do they occur in the endometrium?

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A Well, that's what I was getting to just a moment ago. Some of those changes may already be present in the endometrium. So that would explain why some women -- women -- two women have retrograde menstruation; one gets endometriosis and the other one doesn't, because of those changes already present.
Q Have you witnessed any of those cell changes in any kind of laboratory study or experiment?
MS. AHERN: Objection. Form.
THE WITNESS: Again, could you please rephrase what you mean by that.
BY MR. DEARING:
Q Well, let's say endometrial cells that don't already have some carcinogenic process taking place --
A Okay.
Q -- get -- you know, get free from the endometrium, go through the fallopian tubes, implant on the ovary.
Are those cells capable of turning into endometrioid carcinoma?
A Well, the -- based on that study -- there are a couple studies now -- it apparently doesn't occur. Or that's the suggestion, that it only occurs in women who have this genetic alteration to begin with. Because, otherwise, as we said, women -- many -- not

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many -- more normal women can have retrograde menstruation and don't get endometriosis.
Q And using this diagram again, we were talking about tubal ligation.
A Uh-huh.
Q Where do tubal ligations typically take place surgically on the fallopian tube? Just anatomically, are they --
A Yeah.
Q -- on the distal end, or is it closer to the -- close to the uterus or where -- where are they usually ligated?
A It can vary depending on when these are done, for example, laparoscopically, where the surgeon finds a good place to pick up with his forceps some fallopian tube to tie it off. So sometimes it's in the middle. Sometimes it's more distally. It's more often in the middle. That's what people aim for, rather than in the proximal end, which would be the end closer to the uterus.
Q And the reason that tubal ligations reduce a woman's risk of ovarian cancer is because, if you ligate or close these tubes, endometrial material and potential environmental carcinogens are blocked and cannot pass through the fallopian tubes and reach the

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fimbriated ends of the tubes and the ovaries; is that a fair statement?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I didn't say anything about other than blood and endometrial products that are in retrograde menstruation, and those are -- tend to be associated to a greater extent with clear cell and endometrioid carcinoma rather than high-grade serous carcinoma.
BY MR. DEARING:
Q Right. Were you taking exception to something I said in that statement?
A Yes.
Q Did I --
A Well, do you want to repeat the statement --
Q Sure.
A -- and I'll point out where I'm differing.
Q The statement is, if you ligate or close the fallopian tubes, endometrial material and potential environmental carcinogens are blocked. They cannot --
A Stop. That's where I was disagreeing. "And potential environmental carcinogens," I didn't agree with that. I agreed with the blood but not with that part.
Q What about environmental carcinogen -- what

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about that statement do you disagree with?
A Well, I don't know that environmental carcinogens have ever been demonstrated to go in retrograde menstruation.
Q Is that one of those situations where it's not biologically plausible to you that tubal ligations would reduce potential for environmental carcinogens to reach ovaries because you haven't seen it?
MS. AHERN: Objection. Form.
THE WITNESS: I think it's speculation because I don't think there's been evidence produced to demonstrate that there are other environmental carcinogens or whatever that are coming into the uterus.
BY MR. DEARING:
Q Doctor, this is your sixth edition of Blaustein's.
A Ah, yes.
Q You recognize it?
A Yes.
Q This is the most current edition; right?
A Currently, that's right.
Q I'm sorry. I don't have six copies of this. It's very heavy. But I do want to ask you about something.

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A Okay.
Q So I'm referring to Chapter 14 of this book. And Chapter 14 is entitled "Surface Epithelial Tumors of the Ovary."
You're familiar with this chapter; right?
A Yes.
Q And you're one of the authors of this chapter; right?
A Yes.
Q On page 681 of this chapter, you're discussing, for context, etiology and risk factors for ovarian cancer; right?
A Well, I'll have to see. I can't read it from there.
Q Well -- all right. So this is the title page, "Surface Epithelial Tumors of the Ovary."
And you see the first section says "Epidemiology"; right?
A Well, I can't. Maybe you can magnify it greater.
Q Maybe.
A I can see "Surface Epithelial," but I can't see the subheadings.
MS. AHERN: I think part of it is the glare from the lighting is making it a little hard to read.

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THE WITNESS: That's better.
BY MR. DEARING:
Q Okay. It'll be easy for you to read along with me, but...
So this is the chapter on surface epithelial tumors of the ovary.
A Correct.
Q And then the first few pages discusses epidemiology; right?
A Yes, it does.
Q Okay. And then over here, one of the first sections it talks about is etiology and risk factors.
See that at the bottom there?
A Yes.
Q Okay. Then I'm going -- I'm only showing you that to show you that's the section that we're in.
A Okay.
Q I'm flipping over to the next page, which is 681. And at the bottom of 681, you see it says "Reproductive Factors."
And then this is the part I want to read to you. So we're talking about etiology and risk factors and, within that heading, reproductive factors. And you say:
"In addition, hysterectomy and

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tubal ligation prevent the introduction of a variety of potential environmental carcinogens from entering the peritoneal cavity and thereby coming into contact with tubal and ovarian tissue."
That's where I got that statement from.
So are you now saying you disagree with your statements in this textbook with regard to environmental carcinogens?
A Well, you have to understand textbooks. You basically cite what's out there. And what we're stating there is what some people have allegedly reported, so that we're trying to be complete.
Q No, Doctor, that's not what somebody alleged in a report. That's the predominant theory. That's why that's in the textbook.
You're not saying this is what a few people say. You're saying this because this is the predominant theory; right?
A I didn't say --
MS. AHERN: Objection. Argumentative.
THE WITNESS: I didn't.
MS. AHERN: Object to the form.
THE WITNESS: Sorry.
I didn't say anything about the predominance.

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I said it's a view that's out there and that's reported. I didn't say anything about -- that it's the predominant.
BY MR. DEARING:
Q It wouldn't be in this textbook and written that way if it wasn't biologically plausible, would it be?
MS. AHERN: Objection. Form.
THE WITNESS: I'm not getting into biologically plausible. We've already discussed that. It's been described by some people. So in fairness to those other reports, we've included it in the chapter.
BY MR. DEARING:
Q But you didn't even cite to anybody else. There's no cite there.
A It's kind of a general statement.
Q So it's your testimony that you put that statement that tubal ligations and hysterectomies offer protective effect against environmental carcinogens because a few scientists have said that?
MS. AHERN: Objection. Form. Argumentative.
THE WITNESS: I didn't say "a few" or whatever. I just said it's out there. So I -- we mentioned it. We included it.
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BY MR. DEARING:
Q Do you agree with me that, with regard to this statement and the protective effect of hysterectomies and tubal ligations against the introduction of environmental carcinogens, that there's no qualifying language associated with this statement like "I don't really believe this" or "This is an outlier-type opinion"? There's nothing like that in that statement, is there?
A That's true.
Q And this textbook, which you just said is for doctors, medical students, scientists, people that want to know, if they wanted to know what's -- you know, does hysterectomy and tubal ligation offer protective effect against ovarian cancer, they would look to your textbook.
And all it says is it does offer protective effect against environmental -- potential environmental carcinogens; right?
MS. AHERN: Objection. Form.
THE WITNESS: It's --
BY MR. DEARING:
Q In other words, there's no alternative view stated there, is there?
MS. AHERN: Objection. Form.

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THE WITNESS: What's stated there is what's stated there, yes.
BY MR. DEARING:
Q Okay. While I have the book open, I asked you a specific question about whether you agreed that retrograde menstruation is a common physiologic process that occurs in 90 percent of menstruating women with normal unoccluded fallopian tubes, and you said you think that it's a lot of women or it's a majority.
A Yeah, it is pretty high.
Q Well, would it surprise you that that 90 percent came from your textbook?
A Well, I'd like to see it.
Q Okay. On page 642 where you're describing endometriosis, see there, and usual sites?
A I see that.
Q The next column over where I have the blue marker, it says:
"Retrograde menstruation through the fallopian tubes is a common physiologic process occurring in 90 percent of menstruating women with patent tubes."
Do you agreed with that statement?
A Well, can I -- I can't read that. I want to see if you can make it --
Q Sure. There you go.
A Yeah, that's what it says.
Q Okay. I wasn't trying to trick you.
A Well, I just want to be sure if it's correctly stated.
I have to make a minor equipment change here. Okay.
Q This textbook was published in 2011; right?
A That's correct.
Q So it was published before you were retained as an expert by Johnson & Johnson; right?
A Correct.
Q Do you agree that if talc can reach the uterus, then it could reach the ovaries?
A I don't --
MS. AHERN: Objection. Form.
THE WITNESS: I don't agree that talc can reach the uterus.
BY MR. DEARING:
Q Right. I'm just asking you hypothetically, if talc could reach the uterus, then do you think it could also reach the ovaries, either through retrograde menstruation or some other process?
MS. AHERN: Objection. Form.

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THE WITNESS: Again, there's no data. I have no -- no data, so I can't say that it could.
BY MR. DEARING:
Q Well, I'm asking you as a 40-year experienced gynecologic pathologist. Okay. Relying on all the experience that you've -- relying on all of your experience, do you have an opinion either way whether, if talc could reach the uterus, then it could probably reach the ovaries?
A Pure speculation. I can't comment on that.
Q Well, you're an expert. You are allowed to speculate.
A Doesn't matter if I'm an expert. It's speculation.
Q Okay. So you --
A It's meaningless.
Q So you don't have an opinion either way?
A I told you I don't think it could reach the uterus, and I don't -- and, therefore, I don't think it can go any further. It can't get to the uterus.
Q If it was implanted in the uterus, do you think could reach the ovaries?
MS. AHERN: Objection. Form.
THE WITNESS: Again, show me a study where they've done that, and then I can, you know, intelligently

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discuss it.
BY MR. DEARING:
Q So without seeing a study, you have no opinion either way whether talc could move from the uterus to the ovary?
A That's not science. It's just speculation.
Q Okay. Is retrograde menstruation one of those biologically plausible ideas that you do believe exists even though you haven't seen it take place?
MS. AHERN: Objection. Form.
THE WITNESS: Wait. I'm sorry.
BY MR. DEARING:
Q You have testified you've never seen retrograde menstruation take place, but you do say that it's biologically plausible.
A Well, I said, in fact, that I've seen, in microscopic sections of the fallopian tube, parts of endometrial tissue and blood in the lumen of the fallopian tube. So, yes, I think it can occur.
Q I can't remember if you answered this. If you did, I apologize.
You've said retrograde menstruation occurs during the regular menstrual cycle of a woman. And I said does that mean you're saying it flows both ways at the same time, and you said yes.

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Do you know what specifically causes it to flow upstream, you know, towards the fallopian tube?
A I have no idea. I don't think anyone has.
Q In your report, on page 6, under the section "Precursor Lesions" --
A Yes.
Q -- you state:
"Our understanding of the pathogenesis of ovarian cancer has advanced in the last few years with the recognition that many high-grade serous carcinomas developed from a precursor lesion in the fallopian tube designated serous tubal intraepithelial carcinomas or STIC."
Did I read that right?
A Yes, that's correctly stated as it's written, yes.
Q Do you believe that most high-grade serous ovarian cancers derive from the fallopian tube?
A I do.
Q Can a trained pathologist tell if a cancer derived from the fallopian tube by looking at it under a microscope?
MS. AHERN: Objection. Form.

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THE WITNESS: Well, I should say that, at times, there can be a lesion that comes from another site that mimics serous tubal intraepithelial carcinoma, so you have to be very careful when you draw that conclusion.
BY MR. DEARING:
Q Sir, that's not the question I'm asking.
A Oh, okay.
Q Can a trained pathologist tell by looking at a tumor whether it came from the fallopian tube or whether it originated at the ovaries?
A Well, you can't do it simply on H&E analysis. You really require molecular analysis to demonstrate that it's cloned, that the same genetic alterations that are present in the STIC are present in the -- in the corresponding ovarian cancer.
Q So a surgical pathologist, for example, looking at a surgical specimen from an oophorectomy that's been diagnosed, at least before surgery, as ovarian cancer can't tell if that carcinoma originated from the ovary or the fallopian tube by looking at the tumor; right?
MS. AHERN: Objection. Form.
THE WITNESS: Just looking at the H&E, based on the studies that have been published, I think it would be reasonable to suspect that that's where it came from.

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BY MR. DEARING:
Q But there's no characteristic about the tumor that tells you that; right? There's nothing you can see under a microscope where you could say, "Oh, that came from the fallopian tube versus ovarian primary"?
MS. AHERN: Object.
THE WITNESS: That's correct.
BY MR. DEARING:
Q And when you're using the term "precursor lesion" in your report, what do you mean by that? How do you define "precursor lesion"?
A Well, it's a lesion that precedes the development of, in this case, invasive carcinoma. Because a STIC is a cancer in situ, if you will, but there are other lesions in the p53 signatures which are benign that appear to precede the development of STICs.
Q And you don't believe type 1 tumors originate in the fallopian tube, do you?
A Well, we think possibly that some low-grade serous carcinomas, which are type 1 tumors, may well arise from fallopian tube, but in a different mechanism.
Q Can you give me an example of a fallopian tube precursor lesion that may be a precursor for any type of ovarian cancer?

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A STIC, or p53 signature.
Q So you're saying it is a -- that type 2 tumors start out as serous tubal intraepithelial carcinomas in the fallopian tube, and then somehow migrate from the fallopian tube to the ovaries?
MS. AHERN: Objection. Form.
THE WITNESS: Yes. That's correct.
BY MR. DEARING:
Q What mechanism propels it through the fallopian tube to make it implant on the ovary?
A Well, there may be a number of ways. One way is that these STIC cells have this cohesiveness, so that they are breaking off and they can fall into the fallopian tube and they could migrate up that way, or they might even be -- even though they are noninvasive, there may be a way, it has been suggested -- I'm not sure it is well documented -- it somehow may get into lymphatics and get into the ovary that way.
Q What are some of the causes of fallopian tube precursor lesions?
MS. AHERN: Objection. Form.
THE WITNESS: We don't know what they are.
BY MR. DEARING:
Q Could environmental carcinogens be a potential cause of a tubal precursor lesion?

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A Well, we haven't made that finding yet.
Q If talc could reach the fallopian tubes, could talc serve as a catalyst for a precursor lesion that would create a STIC that might lead to an ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Well, based on what we've seen with talc in other locations, such as when it's used in pleurodesis -- long-term studies have not shown the development of carcinoma -- I don't think it would cause ovarian cancer.
BY MR. DEARING:
Q Well, if -- if foreign bodies aren't causing tubal precursor lesions, can you give me an example of anything that does? Anything that's not bacterial.
MS. AHERN: Objection. Form.
THE WITNESS: It's an area we just don't know. Something causes a p53 mutation -- we don't know what it does, what it is -- and that starts the ball rolling.
BY MR. DEARING:
Q And you think that's a biologically plausible explanation for the carcinogenesis of some ovarian cancers even though you've never seen it?
A May I please --

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MS. AHERN: Objection.
THE WITNESS: Please rephrase the question.
MR. DEARING: Sure.
BY MR. DEARING:
Q You obviously think that this precursor tubal lesion idea that is a precursor lesion for ovarian cancers --
A For high-grade serous ovarian cancers.
Q And some low-grade, you said?
A No, no. It's a different mechanism.
Q Let's stick with high-grade serous. That's the majority of cancers anyway, isn't it?
A Yes.
Q So are you saying that these tubal lesions are -- are you saying it's biologically plausible that these tubal lesions are precursor lesions to high-grade serous carcinomas where they're starting in the tube and implanting in the ovary?
A That's the mechanism we think is at play, yes.
Q And you believe that's a biologically plausible explanation for that process even though you don't know what's causing the tubal lesions; right?
MS. AHERN: Objection. Form.
THE WITNESS: We're saying that we don't know the cause of STIC, but we know that it has mutations and

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morphologic changes that are exactly the same as those in high-grade serous carcinomas. So we're able to make that jump, but we don't know -- we'd love to know what the cause of a STIC is. Prevention is, to me, the only way we're going to make headway and, really, an impact on preventing the development of that. But we have no idea what it is that we need to prevent at this point.
BY MR. DEARING:
Q Could tubal exposure to exogenous or environmental materials cause tubal precursor lesions?
MS. AHERN: Objection. Form.
THE WITNESS: We don't know.
BY MR. DEARING:
Q Well, are these serous tubal intraepithelial carcinomas -- do they derive from inflammation? Or do you not know that either?
A No, I see -- I've looked at a lot of these, and I've never seen inflammation of any type associated with STICs.
Q Are you aware of any reason why a potential environmental carcinogen could not be a cause or a precipitating exposure of a STIC?
MS. AHERN: Objection. Form.
THE WITNESS: Please repeat the question.
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BY MR. DEARING:
Q So you said you don't know, or we don't know, whether environmental materials are causing these STICs.
A Right.
Q Is there any particular reason why it could not be an environmental material causing these STICs?
MS. AHERN: Objection. Form.
THE WITNESS: It is a negative question. I mean, we don't know. It doesn't tell me anything. I still can't really quite figure out what you're driving at.
BY MR. DEARING:
Q Well, let me ask it in the positive form of that question. Is it possible that some of those precursor lesions are caused by environmental materials?
MS. AHERN: Objection. Form.
THE WITNESS: We need to see the data.
BY MR. DEARING:
Q So you can't say yes or no to that question?
A That's right. It's not known.
Q Well, you would agree that it is well known that tubal epithelial inflammation can stimulate proliferation of the epithelium and instigate pathogenesis of tubal hyperplasia; right?

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MS. AHERN: Objection. Form.
THE WITNESS: That's correct. That's in our paper.
BY MR. DEARING:
Q So inflammation can play a role in the development of some precursor lesions within the fallopian tube.
MS. AHERN: Objection. Form.
THE WITNESS: Proliferation isn't the precursor lesion. Proliferation can occur in completely benign conditions. It has nothing to do with cancer.
BY MR. DEARING:
Q Right. But it's the epithelial inflammation that's creating the proliferation of the epithelium; right?
MS. AHERN: Objection. Form.
THE WITNESS: The epithelial -- the inflammation that we describe in our paper on papillary tubal hyperplasia, I think it's important to point out, is due to pelvic inflammatory disease, not due to talc exposure.
BY MR. DEARING:
Q Tell me if you agree with this sentence: "It is well known that an inflammation may stimulate proliferation of tubal epithelium; and, therefore, it is plausible that chronic salpingitis may play a role

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in the pathogenesis of papillary tubal hyperplasia and endosalpingiosis."
A Sounds like it's taken out of my paper.
Q It is.
A Our paper. But, again, we talked about it earlier. That refers specifically to serous borderline tumors, which is a precursor, if you will, of low-grade serous carcinoma, not high-grade serous carcinoma. They're different. They're totally different.
Q Okay. Well, let's talk about low-grade serous carcinomas and borderline tumors.
A Okay.
Q Are you agreeing with me, then, with regard to those tumors that an inflammatory process within the fallopian tube is what stimulates the proliferation of the tubal epithelium?
A That's our hypothesis. That is to say that inflammation virtually -- basically meaning pelvic inflammatory disease due to sexually transmitted disease -- we haven't demonstrated that, but that's our thinking. So it's a hypothesis that we've put out because inflammation of that sort can produce proliferation of tubal epithelium.
Proliferation of tubal epithelium in and of itself doesn't mean it's going to go on to the next

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step, a borderline tumor. You may have tubal proliferation; nothing else happens.
Q Do you have any opinion as to what may be causing inflammation that may stimulate proliferation of tubal epithelium?
A As I said, we're thinking maybe pelvic inflammatory disease, chlamydia, gonorrhea, those kinds of sexually transmitted diseases may account for that.
Q So when you say in your report, "I have participated in a number of studies assessing the characteristics of" --
A Where are we talking about now?
Q I'm sorry. Page 18.
A Okay. I'm at 18.
Q It's near the top.
A Okay.
Q It's right in the middle of the first paragraph.
A Okay. "I have participated." Go ahead, yeah.
Q "I have participated in a number of studies assessing the characteristics of serous tubal intraepithelial carcinomas and have not found them to be associated with inflammation."
That statement is not true if you substituted

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STIC for low-grade serous carcinomas; right?
MS. AHERN: Objection. Form.
THE WITNESS: STICs are precursors of high-grade serous carcinoma --
BY MR. DEARING:
Q I know.
A -- not low-grade.
Q Right. But my point is, even though you say you have not seen STICs associated with inflammation, you have seen low-grade serous carcinomas associated with inflammation; right? That's what we were just talking about.
A We've seen --
MS. AHERN: Objection. Form.
THE WITNESS: Sorry.
We have seen inflammation associated with papillary tubal hyperplasia. That's what that paper shows.
BY MR. DEARING:
Q Well, papillary tubal hyperplasia can be a precursor lesion to ovarian cancer, can't it?
MS. AHERN: Objection. Form.
THE WITNESS: Can be a precursor of borderline tumors, which can then be a precursor -- not all of them. Very few of them progress to low-grade serous

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carcinoma. So it could be, but many of them don't.
BY MR. DEARING:
Q Well, and, of course, some borderline serous tumors progress into invasive serous tumors, don't they?
A They progress to invasive low-grade serous carcinomas, some of them.
Q And they can also implant in other organs, can't they?
A Yes, they can.
Q Incidentally, this paper that we're talking about, the papillary tubal hyperplasia paper that you wrote, it also includes some epidemiology information, doesn't it?
MS. AHERN: Objection. Form.
THE WITNESS: You'll have to tell me -- show me exactly what you are talking about.
MR. DEARING: Actually, you know what? I'm not. Let's move on with this.
BY MR. DEARING:
Q Do you agree that ovarian cancer precursor lesions are rarely seen or observed because ovarian carcinomas typically present in advanced stage and those precursor lesions are obliterated or rendered unrecognizable by the cancer?

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MS. AHERN: Objection. Form.
THE WITNESS: We're again talking about ovarian high-grade serous carcinomas.
BY MR. DEARING:
Q Yes.
A Yes, I think that happens.
Q Okay. So one of the things you said previously was you don't believe talc can cause ovarian cancer because you've seen no evidence that talc causes foreign-body granulomatous reactions in gynecologic tissue; right?
MS. AHERN: Objection. Mischaracterizes testimony.
BY MR. DEARING:
Q Does that mischaracterize your testimony?
A Repeat what you just said.
Q Sure.
You said you do not believe that talcum powder exposure can cause ovarian cancer of any sort because you have not seen evidence of a foreign-body reaction, granulomatous reaction, to talc in gynecologic tissue?
MS. AHERN: Same objection. Mischaracterizes testimony.
BY MR. DEARING:
Q What did I get wrong?
A Yes. Okay.

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Q Is that your testimony?
A Yes.
Q Your attorney doesn't think so.
MS. AHERN: The record will reflect --
BY MR. DEARING:
Q Did I say it right?
MS. AHERN: -- what his testimony was earlier.
THE WITNESS: You said the ovary.
BY MR. DEARING:
Q In fact, you said, "I don't even think it's biologically plausible because I've never seen it." Right? Remember that whole line of questions?
A I've never seen talc, yeah, in association with precursor lesions or high-grade ovarian carcinoma.
Q Right. What you said is you didn't believe talc could cause ovarian cancer because you haven't seen the foreign-body granulomatous response to talc that you would expect to see --
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q -- from talc exposure; right?
MS. AHERN: Mischaracterizing testimony.
THE WITNESS: I think we need to be clear that, even if we saw -- even if we saw talc in the case of ovarian cancer, it doesn't mean that it caused it.

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It's just like I said with the HSV, which all those studies showed HSV and cervical cancer and it was totally wrong. So the fact that you see it in there doesn't mean it's causing them.

In fact, in order to have any kind of -- you've got to focus on early lesions. Those are the precursors. That's where the cancer starts, not in the end product, which is cancer. You can see inflammation, of course, all over the place in a cancer.

BY MR. DEARING:

Q Right. I'm just trying to make sure that I have this fine point of your testimony correct, and that is, is it your opinion that talc cannot cause ovarian cancer of any sort because you have seen no evidence that talc elicits a foreign-body granulomatous response in gynecologic tissue?

MS. AHERN: Objection. Mischaracterizes his testimony.

THE WITNESS: We've seen talc does not cause ovarian cancer. So one has nothing to do with the other.

BY MR. DEARING:

Q Have you observed any precancerous lesions in ovarian tissue?

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A In ovarian tissue, precancerous lesions? Very interesting question. We -- and I say "we," the pathology community -- spent 40 years looking for precursors in ovarian tissue and never found it. So that's why the STIC was such a finding, was such a surprise, and was such a revelation in terms of elucidating the early lesions that could go on to the development of high-grade serous carcinoma.

Q So have you seen precursor lesions in ovaries?

A No.

MS. AHERN: Objection. Form.

BY MR. DEARING:

Q Have you even precursor lesions that are precancerous in fallopian tubes?

A That's what we are talking about. STICs, we think, are precursors of invasive cancer. P53 signatures in the fallopian tube are precursors, in some instances, of STICs.

Q And when you're observing the STICs, are you observing them in the fallopian tube or in the ovary?

A In the fallopian tube.

Q So back to my statement. Do you agree that ovarian cancer precursor lesions are rarely seen or observed because ovarian carcinomas typically present in advanced stage and those precursor lesions are

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obliterated or rendered unrecognizable by the cancer?

A Can be.

MS. AHERN: Objection. Form.

THE WITNESS: Can be.

BY MR. DEARING:

Q Can be what?

A Can be obliterated. Not in all cases. Most of the cases you see it -- or many of the cases you see it. Some cases you don't, so we've come to the -- well, we've done a study to show that women who have high-grade serous carcinoma, all stages, with STICs and compare them to women, all -- this high-grade serous carcinoma, all stages without STICs, we've analyzed the molecular genetic features of those carcinomas. They are no different between the ones with STICs and the ones without STICs. Consequently, we think that some of those cases in which you don't see evidence of the STIC was due to overgrowth by the cancer. But a lot of times, the STIC is evident.

BY MR. DEARING:

Q Do you agree that those precursor lesions are rarely seen or observed?

MS. AHERN: Objection. Form.

BY MR. DEARING:

Q That's what the statement says, they are

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rarely seen or observed. Do you agree with that?

A What statement is this?

Q One I've read twice now. I can read it a third time if you would like.

A Read it again, please.

Q Do you agree that ovarian cancer --

A Can you show me where you reading from?

Q Yes. Do you agree that ovarian --

A No, I want to see it.

Q Listen to it first.

Do you agree that ovarian cancer precursor lesions are rarely seen or observed because ovarian carcinomas typically present in advanced stage and those precursor lesions are obliterated or rendered unrecognizable by the cancer?

MS. AHERN: Objection. Form.

THE WITNESS: Okay. Not rarely. I would disagree with "rarely."

BY MR. DEARING:

Q Rarely. Okay.

A Right. In other words, yeah, sometimes you don't see them; many times you do see them.

Q Okay. Turning to page 685 of the same Blaustein textbook you looked at earlier, I'm still in Chapter 14, of which you were an author.

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MS. AHERN: Page -- I'm sorry -- 285?
MR. DEARING: 685.
MS. AHERN: 685. Thank you.
MR. DEARING: I'll try to position this.
MS. AHERN: What year is that edition?
THE WITNESS: 2011, I think.
MR. DEARING: It's the most current.
THE WITNESS: You can see that.
MS. AHERN: Okay. Thank you.
BY MR. DEARING:
Q It's under the subheading "Putative Histopathologic Precursor Lesions." And you write:
"The study of precursors of ovarian carcinoma is difficult because the ovaries are not readily accessible for screening and ovarian carcinomas typically present in advanced stage, obliterating or rendering unrecognizable any precursor lesion that may be present. Furthermore, identification of a putative precursor lesion is based on microscopic examination of a complete resection; and, therefore, the natural history of the lesion cannot be observed."

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So do you agree with that statement as it's written in your textbook?
MS. AHERN: Objection. Form.
THE WITNESS: Can I -- I couldn't really read it. Let me just see it. I'm sure you are right.
So you're talking about the underlined area. Okay. "The study of precursor" --
Well, you read it correctly. That's what is stated. This edition was published in 2011. A lot has changed since then. It is 2019 now. More and more data coming out. And the study that I just mentioned to you, which I think is very persuasive, is that in some instances the precursor lesion is obliterated; however, those cancers -- and that's proven by the fact that those cancers in which we don't see a STIC are the same on a molecular analysis as ovarian carcinomas in which we do see a STIC, suggesting that, in some instances, it's overgrown but not in all by any instance. You know, we've learned a lot since 2011.
BY MR. DEARING:
Q Sure. Well, no matter how advanced the science has become in the last eight years, it doesn't change the fact that most of the precursor lesions get obliterated by the tumor, right, because, by the time they're clinical, most of these poor women are in

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end-stage disease; right?
MS. AHERN: Object to the form.
THE WITNESS: You're said saying "most," and I don't agree with "most."
BY MR. DEARING:
Q You don't agree with "most"?
A No.
Q Okay. Some?
A Some, yeah. Some might be obliterated.
Q Can you put a percentage on how many ovarian cancer cases you've looked at under a microscope where you've observed precursor lesions?
MS. AHERN: Objection. Form.
THE WITNESS: I can't give you a number.
BY MR. DEARING:
Q Is it half?
A I've seen a lot of them. I can't give you -- over the years. I can't give you a number.
Q How about in the last ten years?
MS. AHERN: Objection. Form.
THE WITNESS: Doesn't make any difference. I would see ovarian cancers -- I'd see maybe 30 cases in a week or two weeks. It's a large number of cases. Do I remember how many I've seen with STICs? It's impossible.

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BY MR. DEARING:
Q I'm not asking for a number, but it seems if you observed precursor lesions, that's something that would stand out in your mind, wouldn't it?
MS. AHERN: Objection. Form.
THE WITNESS: Well, not really.
BY MR. DEARING:
Q Are you even looking for precursor lesions when you're doing a surgical pathology evaluation?
A Of course we look for them.
Q So you look for them in every case?
A Every case when the tissue is available, yeah.
Q So you look for them in every case but you have no idea how often you find them?
MS. AHERN: Objection. Form.
THE WITNESS: I can't give you a number.
BY MR. DEARING:
Q So what has specifically developed in the science that changed from "rarely seen" to "often seen" in the last nine -- last eight years?
MS. AHERN: Objection. Form. Mischaracterizes testimony.
THE WITNESS: I didn't -- I'll repeat the same thing again. In some instances, you can see a STIC lesion and a high-grade serous carcinoma. In other

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instances -- and I can't give you a percentage -- you will not see a STIC lesion and a similar-looking high-grade serous carcinoma, which we believe is due to the fact that that STIC lesion has been overgrown by the carcinoma. That's all I can say.
BY MR. DEARING:
Q I should have started with that statement.
So in some cases where you don't see a precursor lesion, do you -- do you still attribute precursor lesions to be the carcinogenesis of the tumor?
MS. AHERN: Objection. Form.
THE WITNESS: Well, based on that study that I mentioned to you a few minutes ago, that's what we're saying, yes.
BY MR. DEARING:
Q Okay. Let's talk about something else.
Do you believe that the introduction of foreign material through the vagina and uterine cavity can cause inflammation and play an important role in ovarian carcinogenesis?
MS. AHERN: Objection. Form.
THE WITNESS: Could you specifically tell me what you're thinking about? What -- what are you referring to?

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BY MR. DEARING:
Q Your textbook, Chapter 14, just past what we read previously.
MS. AHERN: Page? Sorry.
MR. DEARING: Let me find it.
MS. AHERN: Okay.
MR. DEARING: Oh. I was looking right at it and just didn't see it.
BY MR. DEARING:
Q Under your section entitled "Inflammation."
MS. AHERN: Page, I'm sorry.
MR. DEARING: I'm sorry, page 682.
MS. AHERN: Thank you.
MR. DEARING: Chapter 14.
Let me see if I can blow this up so we can all see it.
BY MR. DEARING:
Q It says under "Inflammation" -- and, again, we're in the chapter called "Serous Epithelial Tumors of the Ovary." And specifically, we're talking about etiology and risk factors.
"Inflammation: It has been suggested that inflammation potentially cited by ovulation-induced surface damage by retrograde

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menstruation-induced salpingitis or by the introduction of foreign material through the vagina and uterine cavity plays an important role in ovarian carcinogenesis. Evidence of a pro-inflammatory microenvironment in endometriosis supports this hypothesis for type 1 tumors. High-grade serous carcinomas are associated with chronic salpingitis in 53 percent of cases significantly more often than 23 percent seen in nonserous tumors, lending circumstantial support to this hypothesis."
So this hypothesis about inflammation, and particularly the part about introduction of foreign material through the vagina and uterine cavity, is that a plausible mechanism for inflammation?
A Let me -- I can see it, but --
Q The entire section.
A Yeah, yeah. I just want to check this out.
I see these references.
Q By the way, I'm not disagreeing with you -- with that statement.
A I notice the first reference is from Ness,

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who's written on this subject. And I don't say I entirely agree with her. In fact, I don't.
287 -- who has been an expert witness for plaintiffs.
287...
Q Did you believe her before she became an expert witness for plaintiffs?
A No.
287. Gee, you know, I'm not sure that that reference is correct. I'd have to read the article specifically because it's -- the title of the article is "The Fallopian Tube: Primary Site of Most Pelvic High-Grade Serous Carcinomas." It doesn't say anything about retrograde menstruation, but anyway. So it would be nice to see that reference.
And then, finally, evidence of -- type 1 tumors. Let's see, 95. Okay.
So your question, yes, that's stated. I said that there's problems with the -- with the references.
Q Right. But the studies that pertain to that topic that are referenced here, that is the proposition of those studies, right, that those three things, either the ovulation-induced surface damage or the retrograde menstruation or the introduction of foreign material through the vagina and uterine cavity, play an

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important role in ovarian carcinogenesis?
A I have to remind you that the inflammation that is described there is entirely different from the inflammation induced by talc, one being -- the latter being a foreign-body giant cell reaction and this being the usual type of chronic inflammation.
Q Well, you use the words "introduction of foreign material through the vagina and uterine cavity." So it may not be talc, but you're talking about a foreign material that would evoke the kind of response you're talking -- the kind of foreign-body reaction you're talking about; right?
MS. AHERN: Objection. Form.
THE WITNESS: I'll have to say that it's in there. It's quite speculative.
BY MR. DEARING:
Q All right. Did you believe that to be true in 2011 when you published this book?
A Well, you know, again, what was in there was what we felt at the time.
Q By the way, the Ness study --
A Yeah.
Q -- that it cites --
A Yeah.
Q -- is a talc study, isn't it?

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A I'll have to read the article.
Q You would at least agree that the introduction of foreign material through the vagina and uterine cavity was biologically plausible to you when you wrote it, right, or you wouldn't put it in your textbook?
MS. AHERN: Objection. Form.
THE WITNESS: Again, as I said, a textbook reflects the general consensus of what's out there.
BY MR. DEARING:
Q Okay.
A It may not necessarily reflect my own personal opinion about it because we have to be fair and acknowledge what's out there.
Q So the general consensus out there is that the introduction of foreign material through the vagina --
A I didn't say the general consensus. I said --
Q You did. Those were your words.
A Well, I misspoke.
I said that there -- those studies are out there; people believe it, and that's what was reflected in the textbook.
Q There are also studies out there that -- presumably, that suggest that particles can't migrate through the vagina.
A That's true.

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Q So -- but you chose to cite the articles that do support that proposition that these foreign particles can migrate through the female genital tract; right?
A That's what --
MS. AHERN: Objection.
THE WITNESS: -- was --
BY MR. DEARING:
Q You don't even reference the ones that don't suggest that, do you?
MS. AHERN: Objection. Form. Misstates what the actual text says and what his testimony has been.
BY MR. DEARING:
Q You didn't offer the -- any alternative suggestion in this short chapter on inflammation that suggests foreign materials cannot pass through the vagina and uterine cavity; right?
MS. AHERN: Objection. Form. That's a section on inflammation, not migration.
MR. DEARING: I'm sorry. I meant to say "inflammation."
THE WITNESS: Again, the inflammation is not the type that we see with talc.
BY MR. DEARING:
Q Do you agree, over time, that chronic

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inflammation in gynecologic tissue can cause DNA damage and maybe cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Could you be more specific and repeat that question.
BY MR. DEARING:
Q Do you believe that, over time, chronic inflammation in a particular part of gynecologic tissue can cause DNA damage and result in some type of gynecologic cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Well, when we -- when we talk about causation and initiation of cancer, it has to be viewed at the earliest stage, at a nonlesion that, as a result of, in this case, inflammation, undergoes neoplastic change.
You can see inflammation in well-formed tumors that can be associated with factors that -- cytokines or chemokines, whatever -- that participate in the progression of a tumor, but that's not initiation. That's not causation. And that's what we're really talking about.
BY MR. DEARING:
Q Do you believe that, with regard to peritoneal malignancies, apart from asbestos, radiation, chronic

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inflammation, organic chemicals, and nonasbestos mineral fibers may be etiologic agents in some cases?
MS. AHERN: Objection. Form.
THE WITNESS: Are you reading this from someplace?
BY MR. DEARING:
Q I'm reading it right off my outline regarding --
A Yeah. But does your outline come from something?
Q It comes from several places, but let me ask you the question again if you didn't get it.
I'm referring to peritoneal malignancies. Okay. Aside from asbestos, radiation, chronic inflammation, organic chemicals, and nonasbestos mineral fibers may be etiologic agents in some cases.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Do you agree with that?
A I'd like to see where you're quoting that from.
Q Do you agree with that statement or not?
A I want to see what you're quoting. I'm not going to just make a comment.
Q You don't have an opinion about it?
MS. AHERN: Check the prompter because I think that

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your sentence is incomplete, which is what's confusing him and me.
Can you go back up.
MR. DEARING: I can ask the question again.
MS. AHERN: Go back up and take a look at it in writing. It might help.
MR. DEARING: Okay. Let me ask this question again.
BY MR. DEARING:
Q I think I asked it right the first time, so I'm going to say it slowly.
With regard to peritoneal malignancies -- okay? Talking about peritoneal malignancies. Aside from asbestos -- well, do you believe asbestos can cause peritoneal malignancies?
MS. AHERN: Objection. Form.
Type?
THE WITNESS: That's controversial. It's not clear.
BY MR. DEARING:
Q Do you have an opinion either way whether --
A I'm not -- it may or may not. I don't think that the data is sufficiently robust to make a comment like that -- a definitive comment like that.
Q Well, do you believe chronic inflammation or

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nonasbestos mineral fibers may be an etiologic agent of some peritoneal malignancies?
THE WITNESS: What --
MS. AHERN: Objection. Form.
THE WITNESS: I'm sorry.
MS. AHERN: Go ahead.
THE WITNESS: What peritoneal malignancies are you talking about?
BY MR. DEARING:
Q Any peritoneal malignancies. Think of any kind you want.
A The only peritoneal malignancy is malignant mesothelioma. That's the only one there is.
Q Well, maybe I'm coming at this the wrong way.
How do you define the phrase "etiologic agent"?
MS. AHERN: Objection. Form.
THE WITNESS: How do you define it?
BY MR. DEARING:
Q Well, let's find out.
I'm looking at Chapter 13 of your book, which is written by Dr. Julie Irving and Dr. Philip Clement.
Did you edit this chapter?
A Well, I edited the textbook.
Q Did you edit this chapter?

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A I may -- you know, there was three of us, as I mentioned. I'm not sure if I edited that chapter or one of my other co-editors edited it.
Q In this chapter, under the subheading "Malignant Mesothelioma" is described "clinical features." And in the third paragraph of that section, starting with "More than 80 percent," that's referring to a study. Halfway through that paragraph, it says:
"Asbestos fibers, however, have been identified with special techniques in some of these women."
And they're talking about the malignant mesothelioma patients.
"Aside from asbestos, radiation, chronic inflammation, organic chemicals and nonasbestos mineral fibers may be etiologic agents in some cases."
So in that sentence, what do they mean by "etiologic agents"?
A Good question. I'm not sure what they mean. I mean, do they mean they're just present there or do they cause it? Not clear to me.
Q If you were to use the term "etiologic agent," what would it mean to you?
A Well, I've never -- I can't remember using it

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in that context. I don't use it. It's not something I use.
Q Would you consider asbestos to be an etiologic agent of mesothelioma?
A In some instances, it might be, yes. But in some instances it's not been demonstrated. It's been much more clearly demonstrated in the pleura than it has been in the peritoneum.
Q Would you agree that the HPV virus is a etiologic agent of gynecologic cancers -- of some gynecologic cancers?
MS. AHERN: Objection. Form.
THE WITNESS: Of cervical cancers and vulvar and vaginal cancers, it is the causative agent.
BY MR. DEARING:
Q So when a scientist or pathologist like yourself uses the term "etiology," you're essentially talking about a causative agent, aren't you?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I just said a moment ago, some may refer to it in that way. I don't necessarily.
BY MR. DEARING:
Q Would you -- how would you use the term "etiology"? What does it mean to you?
A Why don't we just look it up, and we can all

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decide -- agree on it?
Q Okay. I don't want to impose a definition on you.
A Okay.
Q But according to Google --
A Google, huh? That's definitive.
MR. ROTMAN: According to the dictionary --
BY MR. DEARING:
Q Well, let me ask you if you agree with this definition.
Is the medical definition of etiological -- and it says, "causing or contributing to the development of a disease or condition." That's what it meant to me.
Is that what it means to you?
A Causing or what?
MS. AHERN: Contributing.
THE WITNESS: Contributing.
BY MR. DEARING:
Q Causing or contributing to cause a medical condition.
A Causing or contributing?
Q Yes.
A Well, again, contributing isn't cause.
Q I didn't ask you that. I'm asking you what

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etiology means to you.
Do you agree with that definition?
A That definition just said that. It says "causing or contributing."
Q Okay. So let's substitute that word in this phrase.
Aside from asbestos, with regard to malignant mesotheliomas, do you think that nonasbestos mineral fibers may cause or contribute to cause malignant mesotheliomas in some cases?
MS. AHERN: Objection. Form.
THE WITNESS: Interesting they don't reference that point.
BY MR. DEARING:
Q I'm reading it.
A Yeah, I know. I'm saying it's interesting that that point wasn't referenced with a citation.
Q Oh, I got you. Okay.
Well, it's clearly the opinion of the two authors of this chapter; right?
A The two authors, yes.
Q And this is a chapter you edited; right?
MS. AHERN: Objection. Form.
THE WITNESS: Like I said, I'm not sure that I edited it.

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BY MR. DEARING:
Q Okay. I'm sorry. I missed that.
So when you talk about cause or contributing to cause, what's the distinction between those two ideas, in your mind?
MS. AHERN: Objection. Form.
THE WITNESS: "Causation," to me, means that it's an initiating factor in setting the process off. "Contributing," to me, means that possibly the process is in place and it contributes to its further progression.
BY MR. DEARING:
Q So contributing to cause, in your mind, is something that assists the progression of something that already exists?
MS. AHERN: Objection.
BY MR. DEARING:
Q Is that what you're saying?
A I didn't say "contributing." I separated "cause" and "contribution."
Q Okay. I want to talk about "cause" and "contributing to cause."
Is there any distinction between those two terms?
MS. AHERN: Objection. Form. Asked and answered.

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THE WITNESS: Can I see that book again, please. I still can't read that.
BY MR. DEARING:
Q I'm not talking about that section now, but...
A Oh, you're not?
Q No. I'm just generally wanting to get your opinion on --
A Oh, I see.
Q -- "causing" or "contributing to cause."
A Oh, I thought you were referring to that sentence. Oh, so we're not?
Q No. That sentence uses the word "etiologic agent."
A Uh-huh.
MS. AHERN: Whatever you meant by that.
BY MR. DEARING:
Q So in your mind, is there any distinction between contributing to cause something and causing something?
MS. AHERN: Objection. Form. Asked and answered very clearly just two minutes ago.
THE WITNESS: Causation is one issue. Contributing is another. They're not the same.
BY MR. DEARING:
Q I don't mean contributing. I mean

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contributing to cause. Okay? You're only giving me half of the phrase.
MS. AHERN: Objection.
BY MR. DEARING:
Q Is there a distinction between contributing to a disease and -- I'm sorry.
Is there a distinction between contributing to cause a disease and causing a disease? Is there any distinction there?
A To me, yes.
MS. AHERN: Objection. Form.
THE WITNESS: To me, causation is much stronger. Contributing may be involved; may not be. It's much more wishy-washy.
BY MR. DEARING:
Q Do you agree that almost all gynecologic cancers are multifactorial in that they may have more than one cause?
A Yes, that's probably true.
Q Do you believe in the cancer progression model of initiation, promotion, proliferation?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Do you agree that that's a reasonable cancer model?

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MS. AHERN: Objection. Form.
THE WITNESS: Well, I think you've got it twisted around anyway.
BY MR. DEARING:
Q Okay. Well, correct me.
A It starts with initiation, and proliferation may be the next step. And then another step may, after that, be promotion and then progression.
Q So when you use the term "cause" or "contribute to cause," are you referring to the initiation phase of that process or the promotion phase or both?
MS. AHERN: Objection. Form. He's never said that he uses those terms.
THE WITNESS: I don't use "contributing to cause" how you understand it. I'm just saying "causation." That, to me, is initiation, period.
BY MR. DEARING:
Q If gynecologic cancers are multifactorial and they may have more than one cause, do you agree that there may be more than one thing contributing to cause them?
MS. AHERN: Objection. Form.
THE WITNESS: There may be multiple causes for a neoplasm to begin, to get an issue, maybe multiple

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causes.
BY MR. DEARING:
Q So for the last time, breaking down that sentence again, coming back full circle now, do you agree that asbestos can be an etiologic agent of some cancers --
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q -- of some mesotheliomas?
MS. AHERN: Objection. Form.
THE WITNESS: Yes, it may be.
BY MR. DEARING:
Q And do you believe chronic inflammation can be a cause of malignant mesotheliomas?
MS. AHERN: Objection. Form.
THE WITNESS: Again, I'd like to see the data for that.
BY MR. DEARING:
Q So you have no opinion on that without looking at a --
A Yeah, I don't -- I don't agree with that.
Q Okay. And do you believe that nonasbestos mineral fibers can be a etiologic agent or cause of some malignant mesotheliomas?
MS. AHERN: Objection. Form.

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THE WITNESS: Same thing, I don't -- I'd like to see the data that they're alluding to.
BY MR. DEARING:
Q Well, you would at least agree with me that the two authors of that chapter believe that, wouldn't you?
MS. AHERN: Objection. Form.
THE WITNESS: The two authors appear to believe that.
MR. DEARING: Mind if we take a break?
MS. AHERN: Sure.
VIDEO OPERATOR BROWN: Time is now 2:15. Going off the record.
(Recess taken.)
VIDEO OPERATOR BROWN: The time is now 2:34. Back on the record.
BY MR. DEARING:
Q Doctor, you said earlier that you expect that talc exposure would elicit a foreign-body giant cell granulomatous response within the body; right?
A That's correct.
Q Would asbestos fibers invoke that same type of response?
A I really am not an expert on asbestos -- asbestosis, but I'm not aware of it doing foreign

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body -- I really -- best thing not to get into that because it's not something I deal with.
Q Have you ever looked at pulmonary tissue of someone suffering from mesothelioma?
A No, I haven't.
Q So you've never observed asbestos in tissue at all?
A That's right.
Q Well, can you think of any reason why asbestos wouldn't evoke the same kind of foreign-body reaction that talc would?
MS. AHERN: Objection. Form.
THE WITNESS: Different agents do different things.
BY MR. DEARING:
Q Do you think that stroma contributes to the development of ovarian cancer or tubal cancers?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Or STIC?
A It might.
Q How might the stroma contribute to the development of tubal cancer or ovarian cancer?
A Well, in many cancers, there's an interaction between the epithelium and the stroma. So it's certainly possible. I wouldn't rule it out, but I

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don't know.
Q Would you expect the stromal tissue to react the same way the epithelial tissue would react in humans?
A Well, they're different. So I don't know how it would react.
Q If talc can cause p53 mutations in tubal cells, would you expect that it could also cause cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Are you speculating that, or has it -- I haven't seen data to that effect.
BY MR. DEARING:
Q Right. I'm asking -- I'm asking hypothetically right now. If talc could evoke a p53 mutation in tubal cells, do you think that talc could cause cancer in tubal cells?
A Not necessarily.
Q Same with ovarian cells?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q If talc could evoke a p53 mutation in ovarian cells, do you think it could cause cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Not necessarily.

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BY MR. DEARING:
Q You answered both of those questions with "not necessarily."
A Correct.
Q Does that mean you don't know, or does that mean you don't think so, or it could?
MS. AHERN: Objection. Form.
THE WITNESS: Well --
BY MR. DEARING:
Q Let me ask the question again.
A P53 signatures have p53 mutations. They don't all go to STIC. STIC has p53 mutations. They don't all go on to invasive cancers. Just having a p53 mutation doesn't mean it's inevitably going to become cancer.
Q Right. I'm not saying it necessary would become cancer, but if talc can evoke a p53 response in tubal cells or ovarian cells, would that be evidence to you that talc could cause cancer?
MS. AHERN: Objection. Form.
THE WITNESS: No.
BY MR. DEARING:
Q Do you agree that one example of inflammation associated with foreign materials includes macrophages?
MS. AHERN: Objection. Form.

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THE WITNESS: Well, macrophages in tissue become histiocytes, and that's part of a foreign-body giant cell granuloma.
BY MR. DEARING:
Q A minute ago, when I asked you about talc eliciting a p53 response and I asked you whether you thought that would be evidence that talc could cause cancer in those cells, why did you say no?
MS. AHERN: Objection. Form.
THE WITNESS: Because, as I said, having a p53 mutation, in and of itself, does not inevitably mean a tissue is going to become malignant.
BY MR. DEARING:
Q Is it suggestive that a tissue might become malignant?
MS. AHERN: Objection. Form.
THE WITNESS: Not necessarily.
BY MR. DEARING:
Q What does that mean, "not necessarily"?
A As I said, you can have a p53 mutation and have a perfectly benign lesion.
Q You said a while ago that one reason you don't believe talc causes ovarian cancer is because you haven't seen talc elicit a foreign-body granulomatous reaction in gynecologic tissue. Right? Isn't that

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correct?
A No, that's not the reason I don't think it causes cancer.
Q Tell me why you think talc doesn't cause -- can't cause cancer.
A Because there's been absolutely no evidence in the literature that it does.
Q Would you agree with me that foreign materials don't always evoke granulomatous reactions in ovarian tissue?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Or extraperitoneal tissue?
MS. AHERN: Objection. Form.
THE WITNESS: I haven't evaluated other foreign bodies or agents.
BY MR. DEARING:
Q So are you agreeing or disagreeing or do you not know that foreign materials don't always evoke granulomatous reaction on ovarian and extraovarian peritoneal services?
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: I'd like to see the data, and then I could make a decision. I haven't seen it.
///

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BY MR. DEARING:
Q In your textbook in Chapter 12, written by Dr. Irving and Dr. Clement, entitled "Nonneoplastic Lesions of the Ovary," the subtitle "foreign-body Granulomas," the statement is:
"A variety of foreign materials may evoke a granulomatous reaction on the ovarian and extraovarian peritoneal surfaces, potentially mimicking malignant tumor at operation."
So the authors here are a bit equivocal about whether foreign materials will evoke a granulomatous reaction; right? They're saying -- they use the word "may" because it doesn't always happen; right?
MS. AHERN: Objection. Form.
THE WITNESS: "Variety of foreign materials may evoke granulomatous reaction on" -- "may."
BY MR. DEARING:
Q Right.
A That's suggestive, but not definitive at all.
Q So is it fair to say that sometimes they do and sometimes they don't evoke a granulomatous reaction?
MS. AHERN: Objection. Form.
THE WITNESS: I don't even think they say that.

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They just say it might.
BY MR. DEARING:
Q Is it equally true that it might not?
MS. AHERN: Objection. Form.
THE WITNESS: Well, may not.
BY MR. DEARING:
Q Do you agree that whether the body reacts to a foreign particle by macrophage or granuloma depends in part on the body's interpretation of that particle and its size?
MS. AHERN: Objection. Form.
THE WITNESS: I don't know anything about the size business. Size.
BY MR. DEARING:
Q So you are saying that the size of a foreign material is not -- in no way influences whether the body tries to sequester that particle with macrophages versus giant cell granulomas?
MS. AHERN: Object to the form.
THE WITNESS: It may. I mean, different sizes of talc may have -- may induce the same thing. I'm not sure the size is that relevant.
BY MR. DEARING:
Q If a macrophage could engulf a talc particle, you wouldn't expect to see a giant cell granulomatous

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response, would you?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Because the macrophage handles it?
MS. AHERN: Same objections.
THE WITNESS: Well, generally speaking, from what I've read about it, these particles are too large for a single macrophage to envelope it, which results in another macrophage coming along with it and membranes fuse and they engulf the particle.
BY MR. DEARING:
Q Are you referring to talc particles?
A Yes.
Q What's your basis for concluding that macrophages cannot engulf a talc particle?
MS. AHERN: Objection. Form.
THE WITNESS: It's been -- I believe it's been stated -- shown in the literature that the particle might be too large. It's going -- it's going to elicit histiocytic reaction for sure.
BY MR. DEARING:
Q Well, do you agree with me that macrophages may respond to very small particles whereas granulomas may respond to larger particles or larger clusters of particles?

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MS. AHERN: Objection.
THE WITNESS: I haven't seen data that divides it up that way.
BY MR. DEARING:
Q You remember who Dr. John Godleski is, don't you?
A I know the name. I know he's involved in this litigation.
Q Right. He testified in the same trial you did.
A Hmm.
Q And he is a pathologist and a microscopist at Harvard. Well, he's retired, but he spent his career at Harvard.
Have you read any of his publications?
A No.
Q Have you read any of his opinions about talc in tissue, particularly in the size of particles he typically finds in tissue?
MS. AHERN: Objection. Form.
THE WITNESS: He's a pulmonary pathologist, as I recall, knows nothing about gynecologic pathology. Having said that, I don't recall specifically reading his summation of his opinions regarding the size of talc particles.

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BY MR. DEARING:
Q Why do you think he knows nothing about gynecologic pathology if you haven't read his stuff?
A Because he's a pulmonary pathologist. Pulmonary pathologists don't look at gynecologic specimens.
Q Well, he's also a general pathologist, a surgical pathologist, and he has been a -- well --
A Well, I'm not impugning his -- I'm just saying he's not a gynecologic pathologist. Let's put it that way.
Q Okay. Are you aware that the publications he's authored state that the talc particles he typically finds in ovarian tissue, in pelvic lymph nodes is in the 5-micron range, maybe 1 to 10 microns, but average around 5 microns?
MS. AHERN: Objection. Form. Are you talking about publications or litigation reports?
MR. DEARING: Publications.
THE WITNESS: I don't remember reading about the size of the particles.
BY MR. DEARING:
Q If a talc particle found its way into ovarian tissue and it was about 5 to 10 microns in size, you would expect that to be handled by a macrophage,

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wouldn't you, not a giant cell?
MS. AHERN: Objection. Form.
THE WITNESS: You're stating a big "if," namely that it gets into ovarian tissue, which I think is --
BY MR. DEARING:
Q I'm going to show you pictures of it in ovarian tissue in just a minute.
A I don't care if you show pictures of it. I don't think it means it's even there. Biologically, it can be a complete contaminant.
Q So are you saying there's no possible way talc can get into any ovarian tissue?
A Well, it's been described. Let's put it that way. It has been described.
Q What does that mean, "it's been described"? I've been describing it all day.
A It's been described that talc is present in ovarian tissue in users or nonusers, as I remember from the Heller article.
Q We can talk about Heller if you like, but the fact of the matter is if a talc particle gets to ovarian tissue and it's between 1 and 10 microns in size, wouldn't you expect that would attract a macrophage, not a giant cell?
MS. AHERN: Objection. Form.

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THE WITNESS: I don't -- as I said, I haven't read anything about -- specifically about the size of particles and whether it's engulfed by a single macrophage or by a giant cell.
BY MR. DEARING:
Q So if you don't know whether a macrophage would respond to it or a giant cell respond to it, how can you say that talc can't cause cancer because it would evoke a giant cell granulomatous response?
MS. AHERN: Objection. That's not at all what he said.
THE WITNESS: We have to get back to precursor lesions and finding evidence of carcinomatous stimulus in those cells, and those are fallopian tube epithelium, not ovarian cells.
(The document referenced below was marked Deposition Exhibit 6 for identification and is appended hereto.)
BY MR. DEARING:
Q I'm handing you a study by Dr. Sandra McDonald and others, including Dr. Godleski, entitled "Correlative Polarizing Light and Scanning Electron Microscopy for the Assessment of Talc in Pelvic Region Lymph Nodes."
Have you ever seen that study? It's fairly

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new. I don't believe it's referenced in your materials.
A Yeah, I don't think I've seen this.
MS. AHERN: Take your time if you want to read it.
THE WITNESS: What's your question?
BY MR. DEARING:
Q My question is, over on page 3 at the top, Dr. McDonald describes the talc being visualized using polarizing microscopy, and she says:
"Talc is readily visible under polarizing light microscopy where it may be found as both plates and fibrous form and where the particles or fibers are brightly birefringent and often in the size range of 1 to 10 microns."
MS. AHERN: I'm sorry. Do you have a copy of that?
MR. DEARING: I do.
MS. AHERN: Thank you. Page 3.
MR. DEARING: Page 3.
BY MR. DEARING:
Q What she's describing here are talc particles that she's seen in ovarian tissue and pelvic lymph nodes. And she's saying that the size range that she sees and that Dr. Godleski has seen repeatedly is in the 1- to 10-micron range.

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Do you have any reason to disagree with that?
MS. AHERN: Object to the form.
THE WITNESS: I want to go back and sort of read this Materials and Methods a little better.
BY MR. DEARING:
Q If you want to take time and read the whole study --
A No, I'm just reading --
Q -- we can go off the record and you can do that.
A I'm reading materials and methods. I'm up to your paragraph.
Q Keep in mind the question is are these -- one, two, three, four, five, six, seven, eight -- eight scientists reporting finding talc particles in the 1- to 10-micron range in pelvic lymph nodes and gynecologic tissue?
A Okay. So they're finding talc particles in lymph nodes, and do they say ovarian tissues here? Probably. It is mainly lymph nodes, it sounds like. They're focused on the lymph nodes.
Q They are. You're right.
A So they find it in lymph nodes, yes. What's your question?
Q The size of the particles they're finding in

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pelvic lymph nodes are 1 to 10 microns, right, as they report it?
A Yes.
Q And if you would turn over to page 9, Figure 3, there's a photomicrograph.
A Hold on one sec.
MS. AHERN: Take your time. If you need to go off the record, we can.
THE WITNESS: Okay. What were you saying now? I'm sorry.
BY MR. DEARING:
Q Okay. Page 9. There are three photomicrographs. And I just want to talk about one of them.
Do you see the paragraph that starts "Figure 3"?
A I'm on Figure 4.
Q Page 9.
A I see page --
Q Page 9.
A Page 9. Yes. Okay.
Q And the paragraph that starts with the word "Figure 3."
A Yes.
Q Okay. Figure 3 -- and that's the table above,

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but Figure 3 shows "correlative polarizing light microscopy, SEM, and EDX from Case 18 in the digestate study."

Below is some photomicrographs.

"Going clockwise from upper left, Panel A shows polarized light microscopy showing numerous birefringent particles, general size range 1 to 5 microns within the macrophages of the left external iliac lymph node."

Do you see that.

A In Figure A?

Q Do you see where I'm reading from?

A "Going clockwise from upper left Panel A shows polarized light microscopy, H&E" --

A is H&E? It sure doesn't look like an H&E.

"-- shows" --

THE REPORTER: Doctor, if you're reading, I'm not picking it up.

THE WITNESS: I'm sorry.

Figure 3 shows correlative polarizing light microscopy, SEM, and EDX from Case 18 in the digestate study (Table 1). Going clockwise from upper left, Panel A shows polarized light microscopy, H&E, showing numerous birefringent particles, general size from 1 to

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5 micrograms -- microns within the macrophages of the left external iliac lymph node.

BY MR. DEARING:

Q Right. That's what I want to point out to you.

A Yeah.

Q Okay. Do you agree that what the authors are saying there is that the birefringent particles observed in the 1- to 5-micron range are being sequestered by macrophages? Right?

A Okay.

MS. AHERN: Objection. Form.

BY MR. DEARING:

Q Do you agree with that?

A Yeah.

Q If you turn the page, there's another photomicrograph on page 11. And, again, they note in the caption underneath it "Numerous birefringent particles under polarized light microscopy" --

MS. AHERN: Where are you? I'm sorry.

MR. DEARING: Page 11.

BY MR. DEARING:

Q "Numerous birefringent particles under polarized light microscopy within the macrophages of a left external iliac

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lymph node."

So, again, there's another photomicrograph of birefringent particles being sequestered by macrophages; right?

MS. AHERN: Objection. Form.

BY MR. DEARING:

Q At least according to those six, seven authors?

A So what -- I need -- could you read that -- I couldn't follow. I was looking at the pictures. What were you reading exactly?

Q The caption underneath the photomicrograph.

A Oh. The caption --

MS. AHERN: Just read it to yourself so she doesn't have to write it down.

BY MR. DEARING:

Q You can stop after A because that's all I'm talking about.

A Okay.

Q So do you agree with me that that's another photomicrograph showing birefringent particles being engulfed by macrophages?

A Well, honestly, I can't tell from this black-and-white photo what they are. I see polarized light and I -- I see polarized, you know, particles,

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but I don't see what they are.

Q Do you agree that the eight authors are reporting those to be --

A Well, maybe they are. But they reported that. I don't see it. I can't convince myself on this picture that --

Q I'm not asking you to. I'm asking you to agree with me or not that the eight authors of this paper identify these birefringent particles in this photomicrograph as being engulfed by macrophages.

MS. AHERN: Objection. Form.

THE WITNESS: Maybe that's what they say, but they don't -- haven't convinced me in the picture. If I were a reviewer, I wouldn't accept that at all.

BY MR. DEARING:

Q Well, of course not. You would want to see the photomicrograph that they looked at.

A Yeah. I mean, they're showing this picture, but it's a gemish, black and white, some little white particles. I can't tell if it's a macrophage or not.

Q If you will turn next to the discussion section. That's the next page.

A Okay.

Q The scientists write:

"The accurate identification of

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talc in pelvic tissues is important because it documents exposure by demonstrating the presence of talc in these tissues and provides evidence and support of the role of talc in the epidemiological association with ovarian cancer in case-control studies."
A Yes.
Q Do you agree that the evidence of talc found within the tissue being engulfed by macrophages is evidence of talc exposure?
MS. AHERN: Objection. Form. He just said he couldn't tell they were being engulfed by macrophages.
BY MR. DEARING:
Q Well, if you presume those talc particles are being engulfed by macrophages and that these six authors are correct in what they observed --
A That doesn't --
Q -- do you believe that that's evidence of exposure?
A It doesn't convince me. I'm not convinced by these photos, frankly.
Q I'm not asking you to be convinced by the photos.
A Well, there were six authors. Doesn't matter.

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They can be all wrong for all I know.
Q Do you think they're all wrong?
A I have -- I can't see it, and that's what you're asking me. Do I see it and believe it? I don't believe it.
Q One of these authors, by the way, is William Welch that we talked about earlier.
A We talked about him earlier.
Q Do you think he's wrong?
A Well, I don't even know what Bill's role was in this. He may have just said, "Oh, yeah. It was the lymph nodes with something in them."
Q Is it your testimony today that these six authors looked at these photomicrographs and got it wrong --
MS. AHERN: Objection.
BY MR. DEARING:
Q -- and then published it in a peer-reviewed journal?
MS. AHERN: Objection. Form. That's not his testimony. He's already given you an answer to this question.
THE WITNESS: They obviously believe it. I -- if you were -- in -- my opinion is they wrote it, but I don't see it.

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BY MR. DEARING:
Q Okay. Well, presume for me, if you would, that they're right, that they are looking at talc particles in the 1- to 5-micron range being engulfed by macrophages.
Do you agree with me, if they're correct, that that's evidence of exposure to talc?
MS. AHERN: Objection. Form.
THE WITNESS: You know, as -- this -- well, if they've been exposed to talc, by seeing evidence of it in the tissue, could essentially also mean superimposed particles on top of the tissue that could be there as a contaminant. So I'm not convinced.
BY MR. DEARING:
Q Okay. How would it have gotten there as a contaminant?
A Because talc is all over the place.
Q So you're talking about after it's removed from the body?
A Yeah.
Q Okay.
A When you look at a pathology laboratory, the laboratory counters, the paper towels, the ceramics --
Q Right.
A -- it all contains talc.

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Q Of course.
A It could easily be introduced into the specimen.
Q Sure. And is a macrophage going to engulf a talc particle that's been taken out of the body and is sitting on a lab or a paper towel?
A As I said --
MS. AHERN: Objection.
THE WITNESS: -- I can't distinguish that this is in a macrophage. It may be talc particles sitting on top of the macrophage.
BY MR. DEARING:
Q Several times in response to my questions, you've answered with "I'm not convinced."
Is that the burden that you're applying to your opinions in this case is that if you're not convinced, then it's not so?
MS. AHERN: Objection. Form.
THE WITNESS: I can only say what I believe in based on the scientific evidence. In this case, I'm not convinced that the talc particles or the birefringent particles that are being shown in these figures are actually within the tissue as a result of them actually being engulfed or whether they are there as a possible -- as a contaminant.

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BY MR. DEARING:
Q Is that the standard that you're using for causation, that you're not convinced?
MS. AHERN: Objection. Form. Misstates and mischaracterizes his testimony.
MR. DEARING: I don't know what his testimony is. I'm asking him.
THE WITNESS: I told you earlier what I expected to see in causation. And that was a fulfillment of all those criteria that we discussed at multiple times.
BY MR. DEARING:
Q Right. But the fulfillment of that criteria has to rise to a level of a preponderance of the evidence in court, and I want to know what standard you're applying.
Is it until Dr. Kurman is convinced, or is it a preponderance of the evidence or something else?
MS. AHERN: Objection. Form.
THE WITNESS: A preponderance of the evidence, of course.
BY MR. DEARING:
Q Okay. So are you suggesting that applying the preponderance of the evidence to this study, that the preponderance of the evidence suggests these six authors got this wrong, that they're not observing talc

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particles being engulfed by macrophages?
MS. AHERN: Objection. Form. Argumentative. Misstates his testimony. He's already answered this question. This is the first time he's looking at this study. He hasn't reviewed the entire thing.
MR. DEARING: He wasn't asked about preponderance of the evidence.
MS. AHERN: He's told you what his basic opinion is from looking at the study in the last few minutes. That's his opinion.
THE WITNESS: I'm even wondering how they just decide to look at this particular lymph node without mentioning that they saw some kind of funny reaction with the H&E slides that then led them to do polarization. I didn't -- I can't find that.
BY MR. DEARING:
Q It's explained in there.
A Well, maybe you can point it out to me. This is the first time I've seen the article.
Q In the brief skimming through that that you just did and the portions that you read, there was no mention of granulomatous giant cell responses to talc particles, was there?
MS. AHERN: Objection. Form.
THE WITNESS: In my brief skimming, that's what I'm

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saying. I wondered what led them to do polarization of these lymph nodes if they saw nothing. You know, we routinely don't polarize tissues in surgical pathology, as even your expert acknowledged.
So what led them to do -- to do polarization if there was no suspicion based on the H&E slides?
BY MR. DEARING:
Q Right. Well, I'm not really asking you what you're wondering about. I'm just asking you if you saw any statements in there -- and I know you haven't read it word for word, but you spent about 15 minutes skimming over it.
No mention of granulomatous giant cell response to talc particles, is there?
MS. AHERN: Objection. Form. He hasn't reviewed the entire article.
THE WITNESS: From what I read in this 15 minutes, I haven't seen that.
BY MR. DEARING:
Q Okay. I looked through your CV and tried to do a quick calculation. It looks like you've received somewhere in the neighborhood of $6 million in funding from pharmaceutical companies for research in your career.
Does that sound about accurate to you?

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MS. AHERN: Objection. Form.
THE WITNESS: No. I would like to see that.
BY MR. DEARING:
Q Okay.
A Which pharmaceutical companies?
Q Look at your CV, if you like. It's under the title "Pharmaceutical Companies Supported." It looks like the Upjohn Company --
A Wait a minute. Wait a minute. Wait a minute.
MS. AHERN: I'm sorry. What page are you on, David, in the CV?
THE WITNESS: I see it. It's page 58.
MS. AHERN: Thank you.
BY MR. DEARING:
Q Okay. It looks like the Upjohn Company gave you 1.3 million and change for research.
A Wait a minute. You're looking at line 1, right, Upjohn Company?
Q I'm going through the whole thing.
A I see 1993 to 1995. I see 314,540.
Q Keep going. There are other entries for Upjohn.
A Clinical at Wyeth Ayerst, '93 to '98, 59,000.
Randomized clinical -- that's a -- an NCI study.

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Merck, human papillomavirus, '99 to '03, 274,000.
You know, in case you're not aware of it, this money doesn't go directly to me. It goes to the university.
Q I know.
A Okay. You know that.
Q I'm just asking you --
A Merck.
Q -- you've received approximately $6 million of funding for research in your career from pharmaceutical companies?
A Upjohn --
MS. AHERN: Objection.
BY MR. DEARING:
Q Upjohn, Merck, Watson, Wyeth, and Pfizer.
A All going to Hopkins. I don't get money. I don't get paid that amount.
Q Does that number sound about right, though?
A Well, I haven't added them all up, so I'd have to sit here in -- with a calculator and add it all up.
Q How much have you earned testifying for Johnson & Johnson to date?
A Since I was first approached?
Q Yes.

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A A little over $190,000 since 2015.
Q Okay. And you haven't billed for any of your preparation work for this deposition; right?
MS. AHERN: Objection.
THE WITNESS: No. That includes partial billing for this.
BY MR. DEARING:
Q Okay.
A Not entirely, partial.
Q And the next edition of Blaustein's that you said is on the way --
A In press, yeah.
Q -- in press --
A Almost in press.
Q -- are you going to disclose in there somewhere that you are a paid witness for Johnson & Johnson in the talcum powder litigation?
A I'll have to look at that. We don't -- there's some comment about talc, just very similar to what we said there. I don't know that it influenced -- it influenced my -- again, it's a statement of what's out there in the literature.
Q Well, you are -- you've already said that you don't necessarily agree with some of the statements in this version, whether because you just don't agree with

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it anymore or they were someone else's opinions, the other author's opinions.
Are you saying you just -- you don't think it's necessary to inform the reader that you're --
A Well, I'll have to think --
Q -- a highly paid expert witness for Johnson & Johnson?
MS. AHERN: Objection. Form.
THE WITNESS: I'll have to think that out and make a decision.
BY MR. DEARING:
Q Okay. Do you know whether the next Blaustein's edition includes the epidemiology studies, the 25 to 28 studies that show a statistically significant increased risk of ovarian cancer in women who use talc for feminine hygiene?
MS. AHERN: Objection. Misstates the literature.
THE WITNESS: We don't go into that degree of depth. It'll be a comment very similar -- maybe a little bit more elaborate than what we had in the 2011 edition, but it's not going to -- it's not an epidemiological textbook. It's not going to go into all those details.
BY MR. DEARING:
Q As I just mentioned and as you've testified,

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you don't necessarily agree with all of the statements made by other authors in this textbook; right?
A Right. As I said, the book is intended to give a general overview of what's out there. I may not necessarily specifically agree with something. But we felt, in fairness, it all needs to be discussed.
Q Well, it's not all being discussed because you're not discussing both sides of these issues on everything; right?
A What -- both sides of what issues? I mean --
Q Well, for example, when we were talking earlier about -- I don't remember now.
Oh, we were talking about whether chronic inflammation, nonasbestos mineral fibers may be etiologic agents for malignant mesothelioma -- malignant -- perineal malignancies.
And you said, well, that's one position, but you didn't offer the other position that those aren't etiologic agents for peritoneal.
So would you agree with me that you've -- you haven't explained both sides of some of these topics?
MS. AHERN: Objection. Form.
THE WITNESS: Well, we've tried, to the best of our ability, to do so.
///

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BY MR. DEARING:
Q Would you agree that good scientists can have differing opinions about cancer etiology?
MS. AHERN: Objection. Form.
THE WITNESS: That's a very, very general question. But if I frame it within the talc litigation, I would venture to say that a reasonable scientist viewing -- viewing all -- viewing the totality of this data, I don't think anyone would agree to say that talc causes ovarian cancer.
BY MR. DEARING:
Q Are you saying that all of the plaintiffs' experts, the 30 or so plaintiff experts, that you know about, are not good scientists?
MS. AHERN: Objection. Form.
THE WITNESS: I didn't say that.
BY MR. DEARING:
Q Okay. Well, my question is, do you agree with me that good scientists can have differing opinions about cancer etiology?
MS. AHERN: Objection. Form.
THE WITNESS: It's neither good or bad. I'm saying that reasonable people looking at all this data, in my opinion, would not disagree that this is -- that talc causes ovarian cancer.

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BY MR. DEARING:
Q Right. I'm not asking you about this data. I'm talking about cancer in general.
For example, there are good scientists, reputable, knowledgeable scientists that disagree with you about your STIC theory; right?
MS. AHERN: Objection. Form.
THE WITNESS: Not many. Not this day and age. Even your expert agrees with us.
BY MR. DEARING:
Q I know. I'm not saying that. I'm saying there are scientists that don't agree with you.
That doesn't make them bad scientists; right?
A Didn't say they're bad scientists.
Q Do you currently sit on any editorial boards or peer review panels?
A I've taken my -- I retired from those.
Q So, no, you're not currently on any?
A No.
Q When was the last time you sat on one?
A Well, I -- when I retired in June of 2017, I withdrew from the various editorial boards that I was on -- that I was currently on.
Q If you were sitting on a board -- editorial board or a peer review panel and you were given a study

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to review for publication that offered some type of cancer causation analysis that you thought was just biologically not plausible, implausible, would you still recommend that publication -- that study for publication?
MS. AHERN: Objection. Form. Incomplete hypothetical. Other problems.
THE WITNESS: I would ask the author to present more convincing evidence.
BY MR. DEARING:
Q Sure. So you wouldn't -- you wouldn't approve or recommend for publication a study that wasn't biologically plausible, right, in your mind?
A I would like to see the data and the evidence that you're referring to, if there's a specific case for me to answer this very general question.
Q I don't have a specific case. I'm asking you a general question.
The general question is, if you were reviewing a study on some cause of cancer -- and I'm not even using a specific, any cause of cancer -- a cause of cancer that was being purported in a study and you felt like it wasn't biologically plausible, you would not recommend that paper for publication; right?
MS. AHERN: Objection. Form.

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THE WITNESS: I'd like to see the study that you're talking about.
BY MR. DEARING:
Q There is no study. I'm making it up.
MS. AHERN: Objection.
THE WITNESS: Well, I don't want to comment about things that you make up.
BY MR. DEARING:
Q Okay. So you don't have an opinion either way whether -- if you reviewed a study that was suggesting something that wasn't biologically plausible in your mind whether you'd approve it for publication?
MS. AHERN: Objection. Form.
THE WITNESS: You're making these hypothetical questions that, to me, are -- I can't answer that.
BY MR. DEARING:
Q You can't answer the simple question of whether a paper was sent to you to review that you felt offered some theory that was not biologically plausible, in your mind, whether you would recommend it for publication? You can't answer that question?
MS. AHERN: Objection. Form. Asked and answered several times.
THE WITNESS: No comment.
///

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BY MR. DEARING:
Q I thought that was an easy question.
All right. The second half of your report is a criticisms of Dr. Kane.
Do you agree?
A Yes.
Q And were you hired by Johnson & Johnson to offer criticisms of Dr. Kane?
MS. AHERN: Object to the form.
THE WITNESS: No.
BY MR. DEARING:
Q Were you offered by Johnson & Johnson to offer your opinions about Dr. Kane's opinions?
A I was asked --
MS. AHERN: Objection. Form.
THE WITNESS: -- to review Dr. Kane's report and comment on it.
BY MR. DEARING:
Q One of the first things you say in your comments section about Dr. Kane -- on page 12, you write, "Although Dr. Kane offers opinions in a host of areas outside her field, including epidemiology and cancer biology" --
A I'm sorry. Where -- let's be on the same page.

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Right in the beginning. Okay. Go ahead.
Q You suggest in the last sentence of the first paragraph that Dr. Kane is offering opinions in a host of areas outside her field, including epidemiology and cancer biology; right?
A Yes.
Q You would agree with me, wouldn't you, that a pathologist, a learned, skilled pathologist, has a working knowledge of epidemiology; right?
A Working knowledge --
MS. AHERN: Objection. Form.
THE WITNESS: -- is different than expertise.
BY MR. DEARING:
Q I don't think she claimed to be an expert in epidemiology.
A Well, Dr. Kane, in her report -- she's been asked to present pathology of ovarian cancer, as I understand it -- devotes exactly one paragraph to a discussion of ovarian cancer, which is less than a percent of her entire report, and spends nearly 50 percent discussing epidemiology. Doesn't make sense to me.
Q Well, you know how to read epidemiology studies, don't you?
A Yeah.

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Q In fact, your textbooks often lead with a section on epidemiology in every chapter almost, don't they?
A I said that earlier. I said sure, we do that, but I'm not focusing in on an epidemiology review.
Q Well, it's full of epidemiological data, isn't it?
A Yes, yes, yes.
Q Okay. And, in fact, in one of your previous editions, in the fifth edition, you actually have an entire chapter devoted to epidemiology, don't you?
MS. AHERN: Objection. Form.
THE WITNESS: You'll notice we removed that.
BY MR. DEARING:
Q Yeah. But you felt like it was important for pathologists to understand epidemiology, and that's why you put a chapter in this textbook; isn't it?
MS. AHERN: Objection. Form.
THE WITNESS: In the fifth edition. And then we included it in each section in the sixth edition.
BY MR. DEARING:
Q Right.
A Of course, epidemiology is important.
(The document referenced below was marked Deposition Exhibit 7 for

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identification and is appended hereto.)
BY MR. DEARING:
Q I'm going to show you what's marked as Exhibit 7, which is that chapter on epidemiology.
MS. AHERN: Or a page from that chapter?
MR. DEARING: The front page. That's the cover page from that chapter.
MS. AHERN: From the fifth edition?
MR. DEARING: The fifth edition.
MS. AHERN: Okay. Exhibit 7. Do you have an extra copy? Okay. Thank you.
BY MR. DEARING:
Q And, as you can see, it's written by Dr. Mark Schiffman, and it's Chapter 27.
A Yes.
Q And then he leads that chapter -- hopefully, you can read that.
A Well, I'm looking at your handout.
Q Okay. Yeah, even this one's hard to read. I'm sorry. My daughter made that for me a couple days ago. It says:
"Most pathologists are part-time epidemiologists as well. Two medical disciplines are more closely allied than" -- "the two medical disciplines

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are more closely allied than many people realize. Epidemiologists study the distribution and determinants of diseases in human populations. In current medical practices, diseases are often defined by histopathologic diagnoses or by clinical pathologic test values."

Did I read that right?

A You read that correct.

Q And this is a chapter you actually edited; right?

MS. AHERN: Objection. Form.

THE WITNESS: The fifth edition, yes.

BY MR. DEARING:

Q Okay. So there's nothing necessarily inappropriate about a skilled, learned pathologist from discussing pathology -- I mean, epidemiology; right?

A Of course. But the point is she's a pathologist and she spends over half -- nearly half her report on epidemiology and a paragraph on pathology. It doesn't seem right, even though we're part-time epidemiologists.

Q You spent half of your report critiquing Dr. Kane. So I could suggest that's not right.

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MS. AHERN: Objection.

THE WITNESS: Well, that was in order to point out the shortcomings of her analysis. That's all that referred to.

BY MR. DEARING:

Q I just want to make sure it's crystal-clear that you're not suggesting skilled, experienced pathologists, like yourself and Dr. Kane, don't understand epidemiology.

MS. AHERN: Objection. Form.

THE WITNESS: I never said that.

BY MR. DEARING:

Q All right. And would you agree with me that you can't explain cancer pathology and etiology without some understanding and explanation of cancer biology?

MS. AHERN: Objection. Form.

THE WITNESS: Cancer biology and epidemiology all come into play.

BY MR. DEARING:

Q So skilled, experienced, learned pathologists typically do know quite a bit about cancer biology if they are studying cancer; right?

MS. AHERN: Objection. Form.

THE WITNESS: Well, again, there's a difference between a pathologist that's a molecular biologist

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doing bench research and the pathologist who's doing surgical pathology. So, yes, of course, a surgical pathologist is going to be aware and understanding but is not going to have expertise necessarily in cancer biology.

BY MR. DEARING:

Q Well, pathologists have had training in cancer biology, haven't they?

A Well, we read about it, we acquaint ourselves with it, we go to lectures, we know something about it, but we are not experts in it necessarily.

Q And cancer pathology papers often discuss cell biology, don't they?

A Yes.

Q You go on to state that your primary area of expertise is gynecologic pathology.

So tell me, what is your -- well, you've already explained to us what your methodology is. Do you have any criticism of Dr. Kane's methodology as far as her -- I know you disagree with some of her opinions, but do you have any criticism of the methodology she used to go about that?

A Yes.

Q Okay. Tell me what that criticism is.

A Well, one of the main things to start with is

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something we've been discussing during the entire course of this deposition, and that is that it's now generally accepted that high-grade serous carcinoma of the ovary begins in the fallopian tube with a precursor p53 signature, p53 STICs, and not the surface epithelium of the ovary. And she even admits that. But yet all the data that she cites, various biology, the cell cultures and studies that she refers, they're all dealing with the epithelial ovarian tissue, the surface epithelium of the ovary, which is not the precursor of ovarian cancer. So those are not valid.

Q It sounds like you are disagreeing with her opinion as to the carcinogenesis of ovarian cancers if her opinion is they're starting in epithelial cells on the ovarian surface; right?

MS. AHERN: Objection. Form.

BY MR. DEARING:

Q Is that what you're saying?

MS. AHERN: Objection. Form.

THE WITNESS: I'm disagreeing with the studies that she cites to support her opinion that talc causes ovarian cancer are based on studies in which she has not looked at the true precursor of high-grade serous carcinoma. That's what I'm saying.

///

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BY MR. DEARING:
Q Sir, are you saying she's relying on faulty studies to reach her conclusions?
A In -- the studies may not be faulty, just the wrong study. Well, as I've said, the precursors -- you need causation, initiation. We talked about this all morning. Should be looking at the precursor lesion in the organ where the lesion begins.
She's looking at -- she's looking at the ovarian surface epithelium, or at least citing studies that evaluated the ovarian surface epithelium, which is not where these cancers begin. So, therefore, she has selected studies that are inappropriate.
Q Do you have any other criticism of her methodology other than she's looked at --
A Well, we can go through them if you want on every -- you know, one at a time.
Q Let's just talk just generally with regard to methodology. And we can talk -- we will go individually.
A Okay.
Q But from just a general standpoint, you suggested one problem with her methodology is that she's looking at the wrong studies.
A Right.

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Q Any other criticism of her methodology generally?
A Some of the studies themselves may have issues with them specifically. But that, I think, is one of the main problems, if you're trying to present evidence for ovarian carcinogenesis and causation, to select the wrong tissues to be evaluated. Everything else goes by the wayside. If the first part doesn't make any sense biologically, then the rest is of no value.
Q Okay. Let's start breaking it down issue by issue.
One of the first issues you identify -- that you criticize is that Dr. Kane made observations regarding similarities between talc and asbestos and between high-grade serous carcinoma and mesothelioma. We've already discussed the Bradford Hill causation analysis to some extent.
Do you agree with me that this -- that that analogy is also one of those nine considerations of Bradford Hill; right?
A Yes. Analogy is, yes.
Q So with regard to Dr. Kane looking at the wrong studies and your criticism of her methodology, is there anything else that comes to mind with regard to her methodology that you think is inappropriate?

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A Well, you want to begin with analogy? You just brought it up a minute ago.
Q Sure.
A Okay. I can read from my report.
"Dr. Kane overstates the significance of compositional similarities between talc and asbestos. Specifically, Dr. Kane relies on an observed 'chemical similarity' between the two, but the two -- but the fact the two materials have similar chemical compositions does not mean they will have similar effects on the body. For instance, the chemical composition of water is almost identical to that of hydrogen peroxide -- they differ by only one oxygen atom -- but their biological effects are vastly different. Dr. Kane fails to provide any support for her suggestion that compositional similarities between talc and asbestos result in similar biologic effects. While talc and asbestos are both silicate minerals, talc is inert. By contrast, surface reactivity and the

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ability to release free radicals contribute to the pathogenic effects of asbestos."
Do you want me to go on?
Q Can you I stop you there? No, I don't. I just didn't want to cut you off midsentence.
A Okay.
Q I know what your report says. I want to ask you some questions about it.
A Okay.
Q So your criticism of her application of analogy --
A Right.
Q -- the one of nine Bradford Hill considerations --
A Right.
Q -- you think that's a methodology flaw?
A Yes. And also, even -- you didn't want me to go on, but the next is that the analogy between malignant mesothelioma --
Q I'll get to that.
A -- and -- okay.
Q You agree with me that Dr. Kane is not saying that talc and asbestos are morphologically identical; right?

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A She makes that comment at some point, but then she says they're similar.
Q She doesn't say they're identical, does she?
A She may not, but she builds her whole case of analogy on the fact that they're doing the same thing.
Q I think you testified already, you haven't look at talc fibers under a microscope, have you?
A I have not.
Q So you don't know whether asbestiform talc fibers and asbestos fibers are similar; right?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Similar in morphology.
MS. AHERN: Objection. Form.
THE WITNESS: I'm referring to what is easily available in the literature, even for a layman who's not a mineralogist --
BY MR. DEARING:
Q Okay.
A -- that talc and asbestos are very different from a structural standpoint. Structure is more important, in fact, than chemistry in causing biological effects.
Q I'm not talking about chemistry. I'm talking about morphology.

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A Right.
Q They're both needle-like fibers. So they're similar.
A No, they're not.
Q They're not similar at all?
A No.
Q Okay. We already talked about the fact that IARC treats asbestos fibers and asbestiform fibrous talc the same with regard to the carcinogenicity evaluation; right?
MS. AHERN: Objection. Form.
THE WITNESS: Again, there's a lot of confusion in this terminology, and I don't want to get stuck into that.
BY MR. DEARING:
Q I'm not confused.
A You're better than I am.
Q Well, I don't want to confuse you. So let me put it out there again. Maybe you just don't know, but do you know whether IARC has classified fibrous talc, specifically asbestiform fibrous talc, as carcinogenic as it did asbestos fibers?
MS. AHERN: Objection. Asked and answered. And I think this is supposed to be about Dr. Kane's report, and she doesn't mention asbestiform talc when she's

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making this analogy comparison.
MS. GARBER: This is a speaking objection.
MR. DEARING: Thank you. You don't need to do that.
MS. AHERN: Well, it was, I think, appropriate under the circumstances. You are talking past each other.
MS. GARBER: It's not appropriate under CMO 11. You've been doing it all day. You should stop because you're breaking the rules.
BY MR. DEARING:
Q You don't discuss fibrous talc in your report?
A That's right.
Q Is that why you're looking at your report?
A I'm looking at my report, yeah.
Q Okay. So do you have an answer to that question?
A My answer is that talc, as the -- as is reported in the literature, has been indicated in virtually every study to be different than asbestos.
Q It is different.
A I'm not getting into asbestiform or any of that stuff.
Q Okay. I don't know if you know the answer to this question, but when a scientist is using the

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Bradford Hill assessment to determine causal association and that scientist is studying analogy, you agree that analogy doesn't mean that the -- the agents are identical, but what it means is that they are -- they have reasonable demonstrable similarities; right? Do you know that or --
A I'm aware of that, but I don't believe they have reasonable demonstrable similarities.
Q Fair enough.
Do you agree that both fibrous talc and asbestos are both fibrous silicate minerals that cannot be readily absorbed or dissolved by the body?
MS. AHERN: Objection. Form.
THE WITNESS: Talc cannot be easily absorbed and degraded. Asbestos, on the other hand, can penetrate tissues and stay in there for periods of time and get into small areas that can lead to development of mesothelioma.
BY MR. DEARING:
Q And they both elicit a biomechanistic foreign-body response in the body; right?
MS. AHERN: Objection. Form.
THE WITNESS: Again, I'm not aware of asbestos producing a foreign-body giant cell granulomatous reaction. It produces fibrosis.

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BY MR. DEARING:
Q You use the analogy of water and hydrogen peroxide as two things that may look similar that are very different.
Did you come up with that yourself? Because it's actually been used in two opening statements in trials.
MS. AHERN: Objection. Form.
THE WITNESS: Honestly, I have another suggest -- it was actually brought up by counsel, and I totally agreed with it. But I actually had other comparisons that I could have mentioned, which I didn't.
BY MR. DEARING:
Q You go on to say in your report that talc particles are normally plate-like, unlike asbestos fibers. And I assume you read that somewhere; right?
A Yeah, probably in the IARC monograph.
Q But you make no mention of fibrous talc. Do you know that fibrous talc exists?
MS. AHERN: Objection. Form.
THE WITNESS: I've already commented on the business of fibrous talc. I'm not going to get into it.
BY MR. DEARING:
Q I just want to know if you knew about it.

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A Sure, sure.
Q All I'm asking is if you know whether it exist.
A I've known it. I've seen it mentioned. Yeah, sure.
Q So you know about it; you just didn't feel the need to mention it in your report?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I didn't want to go into all those details because I didn't feel that it was necessary. I thought there was sufficient evidence to indicate that talc, as described in the literature, is different from asbestos described in the literature insofar as the biological effects that the two produce.
BY MR. DEARING:
Q In your report on page 14, you state "In any event, although it is well established that" --
A Wait, wait, wait. I see Dr. Kane's claim. Are we worried about that? Where are we?
Q Right. It's about -- one, two, three, four -- five lines down from the top, starting "in any event."
A Oh. Top photograph.
Q Right.
A One, two, three four -- "in any event." Okay. Go ahead.

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Q It says:
"In any event, although it is well established that asbestos exposure can cause pleural mesothelioma (and much less commonly lung cancer), the data implicating asbestos exposure and ovarian cancer is significantly weaker."
When you make that statement about ovarian cancer, you're referring to epidemiological data, right, when you say "data"?
A Pretty much so, yes.
Q So you criticize Dr. Kane for discussing epidemiology, and then you rely on an epidemiological study for -- to support your criticism; right?
A Well, in order to criticize her epidemiological studies, I had to use epidemiological studies.
Q Okay. But you agree that, as we've already seen, the data implicating asbestos exposure and ovarian cancer was strong enough for IARC to make that connection; right?
MS. AHERN: Objection. Form.
THE WITNESS: We've discussed this earlier, and I mentioned the various -- what I felt are shortcomings of that analysis, and it's summarized here. Especially

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when you're comparing it to perineal exposure of talc, we're talking about inhalation studies, we're talking about very high occupational exposures or environmental exposures which are very high. The number of women in these studies is very small, and there's a significant chance that these tumors were not carcinomas but mesotheliomas.
BY MR. DEARING:
Q So several times you keep saying occupational exposure and that exposure was very high. But if you don't believe asbestos can cause ovarian cancer, why does it matter how high the exposure is?
A Well, certain thresholds are required for certain things.
Q Do you think if there's enough ovarian exposure to asbestos, that it might cause ovarian cancer?
A I'm saying that's maybe why they came to that conclusion. They're looking at huge exposures. And, yeah, that may be very significant as opposed to a very minimal exposure.
Q Of course, when Dr. Kane made the observation that high-grade serous carcinoma and mesothelioma have striking morphologic similarities, she also referred to two studies that suggest the same thing; right?

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A I'd have to look at her report, what those two studies are.
Q I actually don't have her report. I'm sorry.
A I can't comment.
Q Well, would you agree with me that high-grade serous carcinoma and mesothelioma, although not identical, they do have significant morphologic similarities?
MS. AHERN: Objection. Form.
THE WITNESS: Lots of tumors have similar morphologic similarities.
BY MR. DEARING:
Q Well, those two are so close that pathologists might have mistaken one for the other for years before histopathologic stains were improved eight years ago.
A I think, if you weren't an expert in gynecologic pathology, that may have been -- that may have been an issue.
Q So are you agreeing me that they're pathologically similar enough to where experienced surgical pathologists may have been diagnosing ovarian cancer when it was mesothelioma or vice versa?
A No. You said -- I said experienced pathologists probably would not have that problem. Inexperienced pathologists might have that problem.

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Q Well, let's quote it exactly, on page 14. You state in the last sentence or so of the first paragraph "Finally, from a pathology standpoint" --
A Wait, wait. I don't see -- where's "finally"?
Q Last sentence, Doctor. You're way below it. First paragraph.
A Oh, the first paragraph.
Q Top paragraph.
A "Finally." I see it.
Q Okay.
"Finally, from a pathology standpoint, there is a significant likelihood that some tumors observed in these occupational studies, which are quite dated, were misclassified due to misreporting on death certificates and lack of immunohistochemical analysis to adequately distinguish peritoneal mesothelioma from ovarian cancer (i.e., peritoneal mesotheliomas were misdiagnosed as ovarian carcinomas)."
So by acknowledging that the pathologists may have misdiagnosed those tumors but then saying but not an experienced -- an experienced pathologist wouldn't make that mistake, are you saying that all the

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pathologists that are referred to in these studies were inexperienced?
A One of the studies that they're describing, they describe using the Danish Cancer Registry, and I have, in fact, done studies with the Danish Cancer Registry. And they report a certain disagreement. I think I came up with 16 percent or something like that. And I said, well, maybe it could even be as high as 20 percent.
Well, you have to understand how these registry studies are done, at least in Denmark where I have direct personal experience. These -- the data that comes in are from every hospital throughout the country of Denmark, and it's based on pathology records, for the most part.
When we did our studies of ovarian tumors, borderline tumors, we requested that the slides be sent in. And they probably did something like that in one of those studies. And I can tell you that in our studies, looking at those cases that had been classified -- I'm talking about the borderline studies -- there was significant disagreement because those pathologists weren't that skilled. They just didn't see enough of these rather uncommon cases to make the correct diagnosis.

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And I suspect a similar thing may have happened with these mesotheliomas. Mesotheliomas are relatively uncommon. Little hospitals throughout Denmark may be seeing one mesothelioma, you know, every five years. So they don't have that much experience. So they may have misclassified them. They may be higher than the 16 percent that they refer to.
That's what I was getting at.
Q So the bottom line is you're speculating that some of these pathologists may have misdiagnosed mesotheliomas for ovarian carcinomas?
MS. AHERN: Objection. Form.
THE WITNESS: I'm basing it on my own experience. Not with mesothelioma, but with the Danish tumor registry, with cases seen by nonexpert pathologists sending in to a central review that there is -- there was misclassification, yes.
BY MR. DEARING:
Q So this is a court proceeding, and in court we're interested in evidence. And do you have any evidence that these pathologists in this study that you're referring to likely misdiagnosed ovarian carcinomas for mesotheliomas?
MS. AHERN: Objection. Form.
THE WITNESS: I said there's a significant

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possibility. I didn't say likelihood.
BY MR. DEARING:
Q What are you basing that on other than -- you said -- well, you're basing that on your experience with Denmark?
A Well, I can -- yes, my experience with Denmark and the Danish tumor registry.
Q Okay. Would you agree with me that the fact that skilled surgical pathologists might be confusing ovarian cancers with mesothelial cancers or mesotheliomas, it suggests that those cancers are sufficiently similar to meet the analogy consideration of Bradford Hill?
MS. AHERN: Objection. Form.
THE WITNESS: As I said, a skilled gynecologic pathologist, I don't think, would make that mistake. I think some of those misclassifications are due to nonskilled pathologists who don't see that much. And, therefore, mesothelioma and -- malignant mesothelioma and high-grade serous carcinoma can be distinguished morphologically and aided also with immunized chemistry.
BY MR. DEARING:
Q Sure. I'm not saying they can't be distinguished. They clearly can be. My question is

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the fact that these surgeons were confusing them for years, apparently, doesn't that rise to the level of analogy for purposes of a Bradford Hill causal association analysis?
MS. AHERN: Objection. Form.
THE WITNESS: You mean pathologists, not surgeons. Pathologists.
BY MR. DEARING:
Q Pathologists, right.
A I don't think it rises to the level necessary to really prove that there's analogy.
Q You also take exception to Dr. Kane's recitation of the evidence that talc-induced chronic inflammation can cause ovarian cancer; right?
A Are we on a specific page of my report or her report?
Q Sure. It's just the next section. "Talc-induced chronic inflammation is a cause of ovarian cancer."
A Okay. All right. Okay.
Q We've already had a lengthy conversation about foreign-body granulomas and foreign-body responses.
A Right.
Q But for support -- well, first, you say "foreign-body granuloma" -- I'm sorry.

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Last sentence of the first paragraph.
A Yes.
Q Actually, that's not it. Wait a minute.
On the next page, second sentence, page 16. You say, "Foreign-body granulomas are what you would expect to find in tissue exposed to noninfectious material like talc and surgical gloves"; right?
A Sutures.
Q I'm sorry, surgical sutures.
And for support of that statement, you cite to a study by Dr. Kabeer Shah in the Journal of Clinical Tuberculosis and Other Mycobacterial Diseases; right?
A Let me see. That's 108. That doesn't seem to be the right reference. Hmm. Oh, 106. Sorry. No, 106 doesn't seem to be correct either.
Am I looking at the wrong part?
Shah here. It should be 95, the reference.
MS. AHERN: I think he's referring to your footnote.
THE WITNESS: Could you please repeat your question and tell me what you're referring to exactly.
BY MR. DEARING:
Q Sure. With regard to your statement, "Foreign-body granulomas are what you would expect to find in tissue exposed to noninfectious material like

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talc and surgical sutures," and you say footnote 108 to support that statement; right?
A Shah, yes.
Q Right. You go down to footnote 108, that's the Shah study?
A Right.
Q Okay. I'm handing you the Shah study that I believe you're referring to.
MR. DEARING: Anybody else want a copy?
I'm going to mark it as Exhibit Number 8.
MS. AHERN: Thank you.
MR. DEARING: Will you give him the marked one so we can be proper about this.
MS. AHERN: Yeah.
(The document referenced below was marked Deposition Exhibit 8 for identification and is appended hereto.)
BY MR. DEARING:
Q Is that the study that you relied on for that statement?
A Yes.
Q And this study is entitled "Histopathologic Review of Granulomatous Inflammation"; right?
A Yes.
Q And Dr. Shah does suggest granulomatous

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inflammation might be associated with talc, surgical sutures, and food material?
A Are you reading something specifically that I should be looking at?
Q Well, sure. On page 3 --
A Okay.
Q -- about a little over midway down the left-hand column --
A All right.
Q -- it starts "Two broad forms."
A Yes.
Q And we talked about these already.
A Right.
Q "Two broad forms of well-defined granuloma exist, defined by their etiology." There's that word again.
Do you know how he is using the word "etiology" in that sentence?
A Yeah. He's dividing them into those that are foreign-body giant cell granulomas and immune granulomas. That's all I can make out of it.
Q So -- okay. And he says, "Foreign-body giant cells are histiocytic reactions to otherwise inert material without an adaptive immune response, for example, suture, talc, and food material"; right?

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A Yep.
Q "A collection of histiocytes surround the foreign material and as single histiocytes are unable to phagocytize the foreign material alone. The foreign material" -- I'm sorry. "The foreign material can be visualized by light microscopy and often exhibits birefringence using polarized light."
So histiocytes are macrophages; right?
A Right.
Q Okay. So what he's saying there is that these giant cells form when macrophages alone cannot engulf the particle; right?
A Well, when a single, I think, macrophage can't, so they join forces to encompass this larger material.
Q So when the material is too big for a single macrophage to phagocytize -- which means to ingest; right?
A Right.
Q So if the particle is too big for the macrophage to ingest alone, more macrophages join in, and then a giant cell granuloma is formed; right?
A Correct.

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MS. AHERN: Objection. Form.
BY MR. DEARING:
Q And in your years of experience, you've never observed -- well, let me ask you, have you ever observed a surgical suture in gynecologic --
A Oh, yes.
Q -- material?
A Yeah.
Q And did they form granulomatous reactions --
A Yes.
Q -- or granulomas?
A Yes.
Q You can actually see surgical sutures and granulomas with the naked eye, can't you?
A You can actually see them with the naked eye, that's right.
Q That's because surgical sutures are quite large compared to talc particles, aren't they?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Well, let me ask you --
THE WITNESS: I would think so, yes.
BY MR. DEARING:
Q Based on Dr. McDonald's study we've already looked at --

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A Right.
Q If the average size of a talc particle in gynecologic tissue that they've studied is in the 5- to 10-micron range, a typical surgical suture is probably a thousand times larger than that; right?
A Sure, it's larger. Sure.
Q Not just larger, a thousand times larger?
MS. AHERN: Objection. Form.
THE WITNESS: I don't know if it's a thousand or 500 or 200 or what. Larger.
BY MR. DEARING:
Q Well, by reference, would you agree that a human hair is about 80 to 100 microns in diameter?
A I honestly have never measured. I don't know.
Q Does that seem unreasonable? I looked it up.
A You looked it up. I haven't looked it up, so I don't --
Q Okay.
A Since I'm under oath, I don't want to say something that may not be true.
Q Okay. Well, I'm just trying to add context to what a micron is in size.
So we're talking about granulomatous responses to surgical sutures that are -- if -- if talc particles and tissue are 5 microns, surgical sutures are probably

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a thousand times bigger than a talc particle; right?
MS. AHERN: Objection. Form.
THE WITNESS: We didn't agree on your -- the decision that they're a thousand times -- but they're larger. Let's put it that way.
BY MR. DEARING:
Q Well, you can't see a 5-micron talc particle with the naked eye, can you?
A No.
Q But you can see a surgical suture with the naked eye?
A Yeah. But I can't extrapolate from that that it's a thousand times larger. That's all I'm saying.
Q Right. It's probably bigger than that, but the point is made.
So when Dr. Shah suggested talc might elicit a granulomatous response, he's referring to very large talc particles, not small 5-micron particles or large clusters of particles; right?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Do you not have an answer to that?
A Oh, I'm sorry. I missed it. What was your question?
Q So when Dr. Shah is suggesting that talc might

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elicit a granulomatous response, he's referring to very large talc particles, like industrial grade, not cosmetic-grade particles that are 5 microns?
MS. AHERN: Okay.
BY MR. DEARING:
Q Or large clusters of particles, he might be referring to those?
MS. AHERN: Objection. Form.
THE WITNESS: Yeah. I mean, I don't see why cosmetic talc can't clump together and form larger particles.
BY MR. DEARING:
Q And, again, the statement that you're using the study to support is that foreign-body granulomas are what you would expect to find in tissue exposed to noninfectious material like talc and surgical sutures.
You are talking about gynecologic tissue exposed to talc, right --
A Yeah.
Q -- when you make that statement?
MS. AHERN: Objection. Form.
THE WITNESS: Sure.
BY MR. DEARING:
Q Okay. Dr. Shah never once mentions talc and granulomatous inflammation in ovarian tissue, does he,

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in this study?
MS. AHERN: Objection. Form.
THE WITNESS: As I recall --
BY MR. DEARING:
Q Or any gynecologic tissue, for that matter?
A Not specifically.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q When he discusses reactions to talc, he's referring to lung tissue that has trapped large talc particles or clusters of particles by either inhalation or surgical pleurodesis; right?
MS. AHERN: Objection. Where are you reading from? In the Shah article?
MR. DEARING: Yeah.
BY MR. DEARING:
Q In the beginning, he describes the organs that he's considering.
MS. AHERN: I'm sorry. The abstract?
MR. DEARING: Maybe.
BY MR. DEARING:
Q Yeah. "The pulmonary system is one of the most commonly affected sites to encounter granulomatous inflammation."
A Okay.

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Q Okay. But the point is he doesn't talk about any gynecologic tissue in his response to talc in this study; right?
A I guess it's because it's so rare.
Q Well, you're using a study to support the statement that foreign-body granulomas will form in gynecologic tissue if they're exposed to talc.
A Right.
Q And you're using a study that doesn't even discuss gynecologic tissue; right?
A There's no reason for me to think that there would be a difference, but --
Q Okay.
A -- he didn't describe it, GYN.
Q Okay. Look on page 5, if you would. And that's a photomicrograph. And the way Dr. Shah describes it is first he identifies a foreign-body giant cell reaction within the lung alveoli, and then he says, "with macrophages engulfing inhaled talc."
A Okay.
Q So what he's saying there is that it's actually macrophages engulfing talc particles, right, not --
A We just said that before. Macrophages are equivalent to histiocytes.

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Q Right. But my point is he includes a photomicrograph of that happening just like Dr. McDonald, Godleski, Welch, that group did in that study that we went over a little while ago; right?
MS. AHERN: Objection. Form. Mischaracterizes the paper.
THE WITNESS: Perhaps so.
BY MR. DEARING:
Q Can you tell from looking at this photomicrograph whether talc particles are being engulfed by macrophages?
A On the H&E slide, I can see it, yes.
Q So you believe that that's being accurately described?
A I can see it, yes. I couldn't see it in that other paper.
Q Okay. So on page 20 of your report, you criticize Dr. Kane for discussing parts of the body that is unrelated to ovarian carcinogenesis, yet --
A What are you referring to now? What paragraph?
Q Anyway -- and if I'm remembering this wrong, feel free to correct me; it's your report. But I seem to recall that you were criticizing Dr. Kane for using studies that didn't pertain to gynecologic tissue, they

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weren't gynecology studies, to support one of her propositions.
Do you remember criticizing her for that?
MS. AHERN: Objection. Form.
THE WITNESS: I know you're having a problem, but I -- that came up different places, so I'd like to see exactly where you're referring so that I can try to respond.
BY MR. DEARING:
Q Well, tell you what. If I have time, I'll come back to that.
A Okay.
Q It's not that important.
A Okay.
Q The fact is many pathologists who have studied talc particles in tissue have recognized macrophages as the foreign-body response in talc particles, not large cell or giant cell granulomas; right?
MS. AHERN: Objection. Form.
THE WITNESS: No. The macrophages form giant cell --
BY MR. DEARING:
Q Right.
A -- foreign-body giant cells.
Q But as evidenced in these photomicrographs and

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presumably those of Dr. McDonald's study as well, macrophages can adequately sequester smaller talc particles; right?
A Well, yeah. And they present that in the article. These are foreign-body granulomas that you're seeing here. These collections of -- all of them together form a foreign-body granuloma.
Q But they're described as macrophages.
A Yeah, but the macrophages form the granuloma.
Q Only when they connect; right?
A No, when they lump together.
Q Right.
A You can see it says "foreign-body giant cell reaction within long alveoli with macrophages engulfing inhaled talc."
So the macrophages inhale the talc or phagocytize it. And as they come together, they form a foreign-body giant cell.
MS. GARBER: I'm just going to object to Ms. Ahern pointing out to the doctor where to look during his testimony. I request that she stop doing that. It's also violating the rules.
MS. AHERN: Well, he's asking about that. I just simply pointed him to what he was asking him about.
MS. GARBER: You pointed him to where he needed to

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look to answer the question, so please stop doing that.
MS. AHERN: Well, the question was misleading. I'm trying to assume that macrophages are different from foreign-body reaction.
MR. DEARING: Okay. Well, make an objection. Don't coach the witness. Okay. Just make an objection. That's what you're supposed to do.
MS. AHERN: Well, stop asking misleading questions.
BY MR. DEARING:
Q The same pathologists that have reported observing macrophages responding to talc particles in tissue also suggest that the reason giant cell granulomas are not formed is because the talc particles are too small and the macrophages can adequately sequester them.
Do you agree with that position?
MS. AHERN: Objection. Form.
THE WITNESS: Please show me the reference that you're making.
BY MR. DEARING:
Q You haven't read any studies that you can recall that say that?
A No, not specifically.
Q Okay. While we're on the topic of macrophages, would you agree with me that macrophages

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can also release reactive oxygen species and reactive nitrogen species when they deteriorate?
MS. AHERN: Objection. Form.
THE WITNESS: Yes, they can.
BY MR. DEARING:
Q Have you taught medical students as part of your career?
A Yes.
Q What did you teach medical students with regard to whether size of foreign particles in any way determines the type of foreign-body reaction to it?
MS. AHERN: Objection. Form.
THE WITNESS: I don't think I ever taught them anything about that.
BY MR. DEARING:
Q Well, you certainly taught them about macrophages and giant cell granulomas; right?
MS. AHERN: Objection. Form.
THE WITNESS: Actually, I don't think I did.
BY MR. DEARING:
Q Okay. Something else you wrote in Blaustein's fourth edition --
Tell you what. Can we take about a five-minute break?
THE WITNESS: Sure.

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VIDEO OPERATOR BROWN: Time is now 4:05. Going off the record.
(Recess taken.)
VIDEO OPERATOR BROWN: Okay. Time is now 4:20. Back on the record.
(The document referenced below was marked Deposition Exhibit 9 for identification and is appended hereto.)
BY MR. DEARING:
Q Doctor, I'm showing you a portion of Blaustein's Pathology of the Female Genital Tract, Fourth Edition, marked as Exhibit Number 9.
Actually, I'm sorry. Can I see that one again. Want to make sure I'm giving you the right one. I'm not.
MS. AHERN: Thank you.
BY MR. DEARING:
Q And, Doctor, this is an excerpt from Chapter 14. It's entitled "Diseases of the Fallopian Tube," and it looks like it was authored by you and Dr. Mazur; is that right?
A It looks that way, yes.
Q Okay. What I want to point out is, on page 376, at the bottom, there's a paragraph that -- well, almost at the bottom, there's a paragraph that

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starts "Rarely."
Do you see that?
A Yeah. Uh-huh.
Q It says:
"Rarely talc or another foreign substance may elicit a foreign-body reaction in the endometrium. Talc may be introduced into the endometrial cavity by instruments contaminated with talc powder or by gloves during a pelvic exam. Patients may be asymptomatic or may have menorrhagia."
Did I pronounce that right?
A Uh-huh.
Q "Microscopically, the extent of the granulomatous inflammatory reaction depends on the quantity of the talc inoculated. The infiltrate is characterized by histiocytes and foreign-body multinucleated giant cells surrounding the talc crystals along with lymphocytes and plasma cells. The crystals appear as refractile, birefringent, needle-like, or fan-shaped splinters in polarizing light."

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So two things I want to draw out of that paragraph.
The first is, you say, "Microscopically, the extent of the granulomatous inflammatory reaction depends on the quantity of the talc inoculated."
So what you're saying there, right, is that the type of foreign-body reaction the body exerts towards talc depends on how much talc is there or the size of the particles; right?
MS. AHERN: Objection. Form.
THE WITNESS: Not the type, the extent.
BY MR. DEARING:
Q By "extent," you mean?
A Amount.
Q Okay. So if there were just a few particles, three or four isolated particles, you know, that weren't right adjacent to each other that were in the 5-micron range or so, would you expect that a macrophage could handle those?
A I cannot -- you know, I can't get down into the specifics of the size. It would be more -- basically, what that sentence means is the more of the inoculum, the more of an infiltrate you'll get. I can't break it down to, you know, three macrophages versus ten, whatever.

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Q Okay. But the extent of the granulomatous response depends on the quantity of the talc present in the tissue; right?
A Right.
Q The other thing I wanted to draw out of that is that the -- when you say, "The crystals appear as refractile, birefringent, needle-like, or fan-shaped splinters in polarizing light," you're talking about talc crystals; right?
A Yes.
Q So if they're needle-like, are you referring to talc fibers?
MS. AHERN: Objection. Form.
THE WITNESS: Talc.
BY MR. DEARING:
Q So you're acknowledging that talc can have needle-like morphology?
A Yeah.
MS. AHERN: Objection. Form.
THE WITNESS: Yes.
BY MR. DEARING:
Q By the way, while we're on it, the fourth edition of Blaustein's -- and I don't have the book, but it actually identifies talc as a risk factor for ovarian cancer; doesn't it?

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A As a what, risk factor?
Q For ovarian cancer.
MS. AHERN: Objection. Form. Is there a question?
MR. DEARING: Yes.
THE WITNESS: Oh, you were asking me to comment on that?
MR. DEARING: Let me ask it again.
MS. AHERN: Actually, let him ask you a question first.
THE WITNESS: Sorry. Yeah, I thought you were telling me.
BY MR. DEARING:
Q I did, and then I put a question mark on the end.
So do you agree with me that the fourth edition identifies talc as a risk factor for ovarian cancer?
A Well, again, I don't have the book, but I'd like to see what I said.
Q You don't recall?
A I don't remember. The fourth edition goes back a few years.
Q Each of your Blaustein's has a chapter on risk factors for ovarian cancer.
What are risk factors?

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A Are you asking for the specific risk factors of ovarian cancer or just in general?
Q In general, what do you mean by "risk factors," the term?
A A factor that increases the risk of someone developing cancer.
Q What are the recognized risk factors for ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Well, it's a little bit of a complicated question in that different people have different opinions as to does -- is there enough data to suggest that this particular factor rises to the level of a risk factor. Some say, "Oh, yes, it does." Others say, "Well, it isn't."
So there are these associations which some like to consider risk factors and some that don't. Some are much stronger than others.
BY MR. DEARING:
Q Can you specifically identify what you think are maybe the three strongest risk factors for ovarian cancer?
A Well, family history, I think, is a strong one. I think genetic history in terms of specifically BRCA mutations is a very strong one. And I think kind

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of a negative risk factor would be the use of birth control pills.
Q By "negative," you mean a protective factor?
A Protective factor, right.
Q One of the statements you make in your report is that you mention talc pleurodesis, and I was just looking to try to find it and I don't see it. But I think you will recognize the statement. It said:
"Further, if the consequence of talc and asbestos exposure were similar, one would expect to find cancer arising in patients who underwent talc pleurodesis."
Remember, that was when you were criticizing her use of analogy of talc and asbestos and high-grade serous carcinoma and mesothelioma in the beginning.
A Yes.
Q My question is: Would you agree with me that talc pleurodesis is typically used to treat malignant pleural effusion and, more often, it's used in end-stage disease?
MS. AHERN: Object to the form.
THE WITNESS: Well, it's also treated in benign disease. It is also used in benign diseases.
///

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BY MR. DEARING:
Q I understand. But the overwhelming majority of pleurodesis procedures are used in malignant end-stage diseases?
MS. AHERN: Objection. Form.
THE WITNESS: It is certainly used in malignant conditions, but I don't know about the overwhelming majority of them.
BY MR. DEARING:
Q Would you agree that the pleurodesis patients who are getting pleurodesis because of an end-stage malignancy typically don't live long enough to study the long-term effects of the talc pleurodesis on them?
A That's probably true.
Q And also the talc used in talc pleurodesis is a different grade of purity than the talc used in body powders; right?
MS. AHERN: Objection. Form.
THE WITNESS: Again, I wasn't going to get into the issue of how much is in there and what the purity is and all that. I defer to a mineralogist.
BY MR. DEARING:
Q And, typically, a pleurodesis procedure is a -- is a one-time administration of a heavy volume of talc as opposed to a slow trickle of chronic exposure;

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right?
MS. AHERN: Objection. Form.
THE WITNESS: Heavy volume, yes. A lot it is put in there.
BY MR. DEARING:
Q It's actually talc slurry that's introduced into the pleural cavity; right?
MS. AHERN: Objection. Form.
THE WITNESS: Yes, that's correct.
BY MR. DEARING:
Q Do you agree with me that there are scientists and physicians that advise against using talc for pleurodesis with patients with nonmalignant pleural effusions?
MS. AHERN: Objection. Form.
THE WITNESS: I've read that there's a controversy, some saying it shouldn't be done and some say it's no problem.
BY MR. DEARING:
Q You think that the split is about 50-50, those in favor and those who warn against it?
A Can't tell. I don't know what the split is.
Q I brought one with me. Since I brought it, I might as well show it to you. Right? Actually, I brought two with me.

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(The document referenced below was marked Deposition Exhibit 10 for identification and is appended hereto.)
BY MR. DEARING:
Q This is publication in the ATS -- in the American Journal of Respiratory and Critical Care Medicine by Dr. Ghio and Victor Roggli.
Do you know Dr. Roggli?
A No, I don't.
Q Well, Dr. Roggli is a pathologist and microscopist who has spent a career studying asbestos and mesothelioma and particularly quantifying asbestos burden in lung tissue.
Does that sound familiar? You haven't heard about him?
A I don't know him, no.
Q Okay. Well, do you agree with me that the next-to-the-last sentence -- I'm sorry, I -- mean the last sentence of the first paragraph reads -- well, the title -- the title of this paper is "Talc Should Not Be Used for Pleurodesis in Patients with Nonmalignant Pleural Effusions." And Drs. Ghio and Roggli state that:
"This dilemma results from a possible increased risk of malignant

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mesothelioma in those patients treated with talc. Consequently, an alternative agent should be employed in any additional" -- I'm sorry -- "in any individual without malignancy requiring pleurodesis."
Then he also cites a reference of case reports of malignant mesothelioma after occupational exposure to talc would suggest a possible -- a potential association.
So do you agree with me that, at least according to this paper, Drs. Ghio and Dr. Roggli advise against using talc for pleurodesis in patients with nonmalignant plural effusions?
MS. AHERN: Objection. Form.
THE WITNESS: Well, that's what they say. They do say that the dilemma is -- in this last two sentences above the first paragraph, they say the dilemma about using it for nonmalignant pleural effusions results from a possible increased risk of malignant mesothelioma in those patients treated with talc.
BY MR. DEARING:
Q Right. In other words --
A Possible.
Q Right. So he is saying there's a possibility

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that talc could cause lung cancers; right?
A Mesotheliomas. I'm sorry. Malignant mesothelioma. We should distinguish carcinoma from mesothelioma.
Q All right.
A He says that at the end. And I do believe -- I think -- I'd have to double-check, but I think there was a letter to the editor from someone who had written extensively on pleurodesis who said -- oh, it's Light. Yeah, Light. References Number 2, Light, RW.
Do you see that one --
Q Yes.
A -- in his list of references?
Well, there's a letter to the editor by Light who says I don't agree with that, that they shouldn't be using talc for pleurodesis in patients with malignant conditions -- nonmalignant conditions because there's never been a reported case of mesothelioma in patients with benign diseases treated with pleurodesis.
Q Light --
A And Light has written a lot of that as well.
Q Right. Doesn't his paper say talc should not be used for pleurodesis in that cite?
A No, I thought he --
Q Look at Light cite Number 2.

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A I think maybe it's an issue, but he -- and very specifically -- did we -- I thought I put that in there. I'd have -- I'd have to look for the reference.
Q Okay.
A But I definitely remember a letter to the editor responding to this saying I have never seen it; it's never been reported in the literature; so I would disagree with the fact that it shouldn't -- that pleurodesis with talc should not be used. I'll be able to find it.
Q You also have a section in your report about precursor lesions. Here it is, page 6.
A Page 6 of my report.
Q Right. I'm sorry. If would you turn to page 12.
A 12.
Q 12.
A Okay.
Q In the first paragraph, second sentence, you state, "Dr. Kane opines that genital talcum powder exposure can cause ovarian cancer based on her evaluation of epidemiological" --
A Wait, wait, wait. You said the second paragraph.
Q I'm sorry. The first paragraph.

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A First paragraph. Okay.
Q Second sentence.
A Second sentence. Okay. "She has produced a lengthy report"?
Q I'm sorry. Third sentence. "Dr. Kane opines that" --
A "That" -- okay.
Q -- "genital talcum powder exposure can cause ovarian cancer based on her evaluation of epidemiological, pathological, biological, and mechanistic evidence."
Is it your testimony that there is no pathological, biological, and mechanistic evidence to support the assertion that talc exposure can cause ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: That's correct. I haven't seen that evidence.
BY MR. DEARING:
Q Further down in the third paragraph, about halfway, it says:
"Dr. Kane does not identify any studies linking the use of talc-based body powders to the known genetic alterations associated with the various

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histologic subtypes of ovarian cancer. And, indeed, I am aware of no such studies."
Would you agree me that many of the epidemiologic studies do assess or analyze the data or divide the data based on exposure and different histological subtypes of ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: They do, and they're pretty inconsistent, yes.
BY MR. DEARING:
Q And when you say "I'm aware of no such studies," are you referring to studies that demonstrate genetic alterations of cells exposed to talc?
MS. AHERN: Objection. Form.
THE WITNESS: I'm saying that there are certain genetic alterations that are involved with the -- with carcinogenesis of the different types -- high-grade serous, low-grade and endometrial clear cell -- and I'm not aware of any studies and she did not -- and Dr. Kane didn't mention them either -- linking talc powders to inducing those genetic alterations.
(The document referenced below was marked Deposition Exhibit 11 for identification and is appended hereto.)

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BY MR. DEARING:
Q I'm showing what is marked as Exhibit Number 11, and this is a study by Drs. Fletcher, Harper, Memaj, Fan, Morris, and Saed. I don't believe this study was identified in either of your reference lists.
Do you know if you've ever seen this study?
A No, I don't remember seeing this study.
Q Well, title of this study is "Molecular Basis Supporting the Association of Talcum Powder Use with Increased Risk of Ovarian Cancer."
A Yes.
Q If you would, take a minute and look at the abstract. The last sentence of the abstract reads:
"These findings are the first to confirm the cellular effect of talc and provide a molecular mechanism to previous reports linking genital talc use to increased ovarian cancer risk."
A I was sort of reading the rest of the abstract. Let me go over it.
Okay. I'm sorry, what was your question?
Q Well, having read the abstract, do you feel like you have a good handle on the general topic of this study?

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A Not at all.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Not at all?
A No. I'd like to see the materials and methods. I'd like that see what they were actually studying. I was looking for that. I couldn't see that.
Q You know, if you're not familiar with it, let's move on.
A I'm not.
Q I want to ask you what you're familiar with. I might come back to it if I have time for it.
A Okay.
Q Back to page 12.
A Yes.
Q Middle paragraph, last two sentences, you state:
"Further, it is unlikely that exposure to a single agent, i.e., talc, could result in the development of such distinctly different neoplasms."
My question is there are examples where a single etiologic agent can cause more than one type of cancer; right?

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MS. AHERN: Objection. Form.
BY MR. DEARING:
Q For example, cigarette smoke can cause several times of cancer; right?
MS. AHERN: Objection. Form.
THE WITNESS: Lung cancer, sure. Yeah. What else?
BY MR. DEARING:
Q It can cause -- it has been linked to liver cancer; right?
A I'm not familiar with that.
Q Well, asbestos can cause mesothelioma and it can cause lung cancer; right?
A It's usually not a significant cause of lung cancer. It's a contributing factor to people who are smokers.
Q Asbestos is?
A Yeah.
Q Okay. Well, I know it usually causes mesothelioma, but asbestos can cause lung cancer; right?
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: I think it's pretty rare. I think it's mostly, as I said, predominantly lung cancer and these -- they can add another factor to it, asbestos, what I've read about it, because I'm not an expert in

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cigarette smoking and lung cancer.
BY MR. DEARING:
Q On page 20 you have a subheading "Detection of Talc in Ovarian Tissue."
A I see it.
Q And this appears to be a criticism of Dr. Kane's recitation of the evidence that talc has been observed in ovarian tissue and other gynecologic tissue.
Is that an accurate summary?
A Yes, uh-huh.
Q Are you saying that that's just not true, that talc has not been observed in gynecologic tissue?
A No. I think in my second sentence, I say, "She then acknowledges that the presence of talc particles found in ovarian cancer tissue does not prove that the talc played a causal role yet argues it is 'consistent with causation and provides additional evidence in support after causal relationship,'" which is -- the whole sentence doesn't make sense to me.
Q Okay. I just want to be clear. You're not taking exception to the fact that she's acknowledging that scientists have observed talc particles in ovarian tissue and other gynecologic tissue?
A Well, in ovarian tissue, for sure.

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Q Are you saying the presence of talc in ovarian tissue has no relevance to the issue of inflammation or ovarian cancer?
A I'm saying it's not evidence that it's causing ovarian cancer.
Q So you -- have you seen studies that identify talc in ovarian tissue?
A Yes.
Q And in those same studies, did they identify a granulomatous or giant cell response to the talc?
A Actually, no. That's the Heller article where she sees it, but she specifically says she doesn't see foreign-body giant cell reaction.
Q Can you reconcile that inconsistency if you think that's how the body should respond to talc?
A Well, I think -- reconcile it is that I don't think the talc is there having any biologic function or is really in the tissue. It's a contaminant, and that's why it didn't produce a biologic reaction.
Q Is it your opinion that all of the studies that claim to recognize or identify talc in ovarian tissue are what -- are really identifying contamination?
A I think it's a significant issue. I can't tell you all of them or not.

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Q The fact is there's not a single study that identifies talc particles in ovarian tissue that recognizes a granulomatous giant cell response to it; right?
MS. AHERN: Objection. Form.
THE WITNESS: As far as I know, that's correct.
BY MR. DEARING:
Q The next section of your report is entitled "Migration of Talc to the Ovaries."
A Okay.
Q And I asked you earlier today if you thought talc could migrate from the perineum to the ovaries and you said absolutely not.
Is that still your position?
A Yes. I don't think it can migrate from the perineum.
Q Specifically what you say is -- you say that Dr. Kane's opinion that talcum powder applied to the external perineum can migrate to the ovaries is unsupported by and contrary to the current data and understanding of ovarian cancer pathology.
A Where were you reading that? I'm sorry. I know I said that, but can you see that -- show me that exactly.
Q No, not without reading the whole thing. But

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I want to ask you a question about it. I know that's your position.
A Yeah.
Q Are you aware that there are many studies that conclude that talc particles can, in fact, migrate from the perineum to the ovaries?
MS. AHERN: Objection. Form.
THE WITNESS: From the perineum?
MR. DEARING: Yes.
THE WITNESS: No, I'm not aware of those.
BY MR. DEARING:
Q Are you aware that the 2007 study by Dr. Cramer states that the presence of talc in lymph nodes provides evidence that talc used externally is capable of migrating into the pelvis?
MS. AHERN: Objection. Form.
THE WITNESS: Could -- do you have that paper, by the way?
BY MR. DEARING:
Q I don't.
A I'd like to see the paper because I think there are issues in there that are important to point out.
Q Okay. The one paper I did bring that I already showed you was McDonald's 2019 paper.

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A Right.
Q Remember?
A This is a totally different one.
Q Right. She said that -- said that the talc migrated to pelvic lymph nodes from perineal application.
A Yeah. I don't see how she came to that conclusion.
So, first of all, the 2007 study -- let me make sure this is the correct. 2007.
Q The one I'm referring to is the pelvic lymph node study.
A "Presence of talc in pelvic lymph nodes of a woman with ovarian cancer and long-term genital exposure to cosmetic talc."
Q Okay.
A Right. The first thing is that it's a case report --
Q Sure.
A -- which doesn't really tell you a lot in terms of scientific evidence. This is just any case, any case report.
Q A case where talc migrated to that lady's ovaries from the perineum; right?
MS. AHERN: Objection. Form.

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THE WITNESS: Where does it say anything about it coming from the perineum? I didn't see that. It could have come from inhalation. I mean, I can tell you, coming from the peritoneum and going to a lymph node sounds totally against any method of lymphatic drainage.
BY MR. DEARING:
Q Do you believe --
A Makes no sense.
Q Do you believe that inhalation of talc can result in the deposition of talc particles on ovarian tissue?
A It hasn't been demonstrated that I'm aware of. It has been talked about.
Q You just said it could have come from inhalation.
A Yeah. And I'm saying maybe that's how it came from, but there's no definite proof. But I don't think it --
MS. AHERN: I think it is in your report. You cited it; right?
THE WITNESS: Case report.
BY MR. DEARING:
Q Well, let me ask you about the two cases that you cite --

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A Okay.
Q -- to support your opinion.
A Okay. Sure. I can't find it.
Q One of them was the Wehner study. Do you remember the title is "On Talc Translocation from the Vagina to the Oviducts and Beyond," Alfred Wehner. I have a copy of it here if you would like.
A Yeah. It would be nice to see the paper so I can --
Q I thought you'd say that.
(The document referenced below was marked Deposition Exhibit 12 for identification and is appended hereto.)
BY MR. DEARING:
Q This is Exhibit 12. This is a paper entitled "On Talc Translocation from the Vagina to the Oviducts and Beyond."
A Okay.
Q It is by Alfred Wehner and Dr. R.E. Weller; right?
A Okay.
MS. AHERN: I'm sorry. Do you have --
MR. DEARING: Oh, you need a copy.
MS. AHERN: Thank you.
///

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BY MR. DEARING:
Q And this is a paper that you cite for support that talc cannot migrate from the perineum to the ovaries; right?
A I'd have to see my report where we say that. I see that we -- we're referring to Venter and Egli and then we go to Wehner. Yes.
Q At the top of page --
A Wehner and Boorman. This is Wehner and Wehner.
Q At the top of page 22, you say "notably Dr. Kane omits" and you mention the Wehner 1985 and Boorman 1995.
A Right.
Q "Wehner examined talc migration in monkeys, receiving repeated introductions of talc to the upper vagina over a period of 45 days.
A Right.
Q Right?
A "No talc particles were found in the uterus or tubes."
Q Right.
A Yes. So they didn't find talc.
Q So what's important I want to point out about

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the study is there were six monkeys studied over a 45-day period with only 30 applications of talc; right? That's in the abstract. That's also in the body, but it is easier to find in the abstract.
MS. AHERN: Objection. Form.
THE WITNESS: Six monkeys received 30 applications. Yeah.
BY MR. DEARING:
Q And each of those six monkeys were at different menstrual cycle places; right?
MS. AHERN: Objection. Form.
THE WITNESS: Don't know that -- where it says that.
BY MR. DEARING:
Q The point is 30 applications over 45 days doesn't replicate long-term human genital talc use, does it?
A No, not at all. So you're suggesting that negative finding supports what?
Q No. I'm suggesting that your citing this study for the proposition that talc cannot migrate from the perineum to the ovaries in a human is misplaced --
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q -- because they're not the same thing.

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A But the point is to try to demonstrate, from your standpoint, that it does get there. And there's no study that shows that. I mean, you're supporting a negative, which, to me, is nothing -- is not really relevant. You want to support a positive.
Q You would agree with me that the cynomolgus monkeys don't menstruate the way humans do; right?
A Oh, I don't know about that.
Q They do menstruate, but it's a different process.
A I don't know why it's different.
MS. AHERN: Objection. Form.
THE WITNESS: I don't know.
BY MR. DEARING:
Q Do you know whether these cynomolgus monkeys experience retrograde menstruation?
A No idea.
Q Right. Also, did you know that, at the time of this study, Alfred Wehner was a paid consultant for Johnson & Johnson?
A No.
Q You also cite the Boorman study for the proposition that talc cannot migrate from the perineum to the ovaries in humans.
And, of course, this is a rat study; right?

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MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Rats and mice. Yes?
MS. AHERN: Same objection.
THE WITNESS: That's right.
(The document referenced below was marked Deposition Exhibit 13 for identification and is appended hereto.)
BY MR. DEARING:
Q In fact, it's a one-page rat study. Here it is, if you'd like to refer to it.
Is this the study you were referencing to support your proposition that talc can't migrate from the perineum to the ovaries in humans?
MS. AHERN: Objection. Form.
THE WITNESS: Let me see. Boorman, Seely. Yes, this looks like the study, 1995. Yes.
BY MR. DEARING:
Q Actually, you criticized Dr. Kane for not mentioning the Boorman study; right?
You say, "Notably, Dr. Kane omits any mention of Wehner of 1985 and Boorman 1991."
A Right.
Q And you think that this study, this Boorman one-page rat study, supports the proposition that

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genital talc use cannot -- that talc cannot migrate from the perineum to the ovaries?
MS. AHERN: Objection. Form.
THE WITNESS: I think it's just supportive of the studies that she quoted that says it does.
BY MR. DEARING:
Q Well, you criticized her study.
A Right.
Q So if it was just supportive, that means it's not supportive at all; right?
MS. AHERN: Objection. Form.
THE WITNESS: So they're both not supportive.
BY MR. DEARING:
Q Okay. Fair enough.
In fact, the authors practically say that in this study; right?
If you look at the last sentence of this one-page report, it says, "In the extrapolation of these data, one should consider limitations relative to the marked anatomical and physiological differences between rodents and humans; right?
Do you see that last sentence?
A I'm sorry. I was looking at something else.
Q It's the last sentence of this paper.
A This Boorman paper?

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Q Uh-huh.
A "In the extrapolation of these data, one should consider limitations relative to the marked anatomical and physiological differences between rodents and humans."
Q Right. So the Boorman paper doesn't really tell you much about whether talc can migrate to the perineum -- from the perineum to the ovaries in humans; right?
A That's correct. Interestingly, by the way, in the earlier comment I made about the Cramer 2007 study, I found the sentence -- I'd have to look it up in the paper, but I say, "I note that Cramer 2007," which is the study that we're talking about, "which Kane relies on for a migration opinion, stated that 'there is no proof that talc used externally reaches the pelvis.'"
Q Right. That's the -- that's the 2007 pelvic lymph node study.
A Yes.
Q Right.
A The one we were talking about just a few minutes ago.
Q Right. And the one I showed you earlier by Dr. McDonald is a follow-up to that study, right, the one that's Exhibit 6?

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A The one that was just published in -- when was it?
Q This one was published this year.
A 2007, that was published. Okay.
Q This is the follow-up to that study; right?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q Well, if you would, go back to Exhibit 6.
A What's Exhibit 6?
Q It's the follow-up to the lymph node study. It's entitled "Correlative Polarizing Light and Scanning" --
A Sandra McDonald.
Q Right.
A Since I haven't read that study, I'd like to read it more carefully, because they don't describe how they -- how they -- what tissues they examined, how these patients were possibly exposed to talc.
Q They do explain all that.
A Where is it?
Q Well, I tell you what. Let's go off the record, and you can take all the time you want to read it and we can talk about it.
A Okay.
VIDEO OPERATOR BROWN: The time is now 5:02. Going

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off the record.
(Recess taken.)
VIDEO OPERATOR BROWN: The time is now 5:22. Back on the record.
BY MR. DEARING:
Q Doctor, have you now had an opportunity to read this study entitled "Correlative Polarizing Light and Scanning Electron Microscopy for the Assessment of Talc in Pelvic Region Lymph Nodes"?
A I have.
Q In the abstract, it sets out sort of the purpose and the methodology of this study. And it says that:
"Perineal talc use is associated with ovarian carcinoma in many case-controlled studies. Such talc may migrate to pelvic organs and regional lymph nodes with both clinical and legal significance. Our goal was to differentiate talc in pelvic lymph nodes due to exposure versus contamination with talc in the laboratory. We studied 22 lymph nodes from ovarian tumor patients, some of which had documented talc exposure, to quantify talc using

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digestion of tissue taken from paraffin blocks in scanning electron microscopy with energy-dispersive x-ray analysis. Talc particles correlated significantly with surface contamination assessments using polarized light microscopy. After adjusting for surface contamination, talc burdens in nodes correlated strongly with perineal talc use.
"In a" -- let me just -- "In a separate group of lymph nodes, birefringent particles within the same plane of focus as the tissues in the histological sections were highly correlated with talc particles within the tissue by in situ, SEM-EDX. We conclude that since talc can be a surface contaminant from tissue collection/preparation, digestion measurements may be influenced by contamination. Instead, because they preserve anatomic landmarks and permit identification of particles and cells in tissues, polarized light microscopy and in situ SEM-EDX are recommended to

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assess talc in lymph nodes."
Do you agree that that's an accurate summary of this study?
MS. AHERN: Objection. Form.
THE WITNESS: Pretty much.
BY MR. DEARING:
Q So one of the things we were talking about before we went off the record so you could read this study was that you said you weren't sure about the exposure of the patients in this study.
And if you would turn to page 2 at the top, it says:
"One exposure of great current medical, public health, and medicolegal importance is the association of ovarian cancers with the use of talc cosmetic products in the genital area. Data related to this association come from epidemiologic studies which identified a clear excess of women with ovarian malignancy who had used talc in their genital area prior to developing cancer compared to control women."
Do you agree with that last sentence of these six scientists that data related to this association

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come from epidemiologic studies which identified a clear excess of women with ovarian malignancy who had used talc in their genital area prior to developing cancer compared to the control women?
A I'm not sure what they mean by "clear."
Q So you don't know how to interpret that sentence at all?
MS. AHERN: Objection. Form.
THE WITNESS: I mean, there have been epidemiologic studies that have demonstrated an association between talc usage and ovarian cancer. I don't argue that.
BY MR. DEARING:
Q And then he goes on to cite an epidemiological study two sentences farther down.
"The most recent summary of the epidemiologic data in 2018" -- I guess at the time he was working -- they were working on this paper -- "found that genital talc may increase the risk of ovarian carcinoma by about 30 percent."
And then he's, of course, referring to the Penninkilampi study.
A That's a relative risk, about 1.3 or something.
Q Do you agree that the Penninkilampi shows a relative risk of 30 percent?

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MS. AHERN: Objection to form.
THE WITNESS: Well, by 1.3, right. I just looked at the abstract on that study, by the way.
BY MR. DEARING:
Q Okay. He goes down to describe the Heller study in that same column. And that's a study that we briefly touched on earlier.
A Uh-huh.
Q But he says:
"A study by Heller was done with digestion techniques followed by TEM" -- that's transmission electron microscopy -- "on ovaries from 24 women having hysterectomy, oophorectomy, for reasons other than ovarian malignancy. The study found talc in approximately half the samples, with no obvious correlation with the genital talc use history, thereby suggesting to the authors that talc exposure may be relatively ubiquitous across the population."
And then he talks about Dr. Cramer's and Godleski's 2007 case report that we were talking about prior to the break. He said:

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"A subset of authors from the present study have previously described a case report in which a woman with serous carcinoma of the ovary had a history of talc usage in her genital area, was demonstrated to have talc in three of four pelvic -- examined pelvic lymph nodes."
So when we were talking about the exposure history in the 2007 Cramer case and you said "I don't know if she used perineal talc," you now do know that that was a perineal talc exposure; right?
MS. AHERN: Objection. Form.
THE WITNESS: Well, she claims to have perineal talc exposure, and then these exposure -- and you find talc in the lymph nodes, but that does not directly prove that it got there through the female reproductive tract.
BY MR. DEARING:
Q But the only evidence of exposure in the 2007 Cramer study is the statement by the patient that she used talc perineally; right?
MS. AHERN: Objection to form.
BY MR. DEARING:
Q You're speculating about any other talc

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exposure; right?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I can't -- yeah. I mean, it doesn't prove necessarily that -- passage through the female reproductive tract. It could have been inhaled.
BY MR. DEARING:
Q Next, it says in the next paragraph:
"In the study reported here, we assess talc in a sizeable set of lymph nodes in the pelvic region representing multiple patients; thus, we expanded on the lymph node analysis in the previous case report" -- talking about the Cramer 2007 report -- "as well as the study of nonmalignant ovaries by Heller, et al., and we examined nodes in 22 patients with various types of ovarian tumors."
So do you agree that this study is in part a -- an expansion of Dr. Cramer's 2007 -- Dr. Cramer's 2007 case report and Dr. Heller's study?
A It's a follow-up, yeah. Okay.
Q Okay. And part of the study here is that they assessed -- in the next column at the top, they assess tissue surface contamination as a factor explaining the high talc burden in some cases as opposed to talc that

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migrated to the nodes from perineal exposure.
So, clearly, they are surmising or suggesting that the talc found in the lymph nodes in this study migrated to those lymph nodes from perineal exposure; right?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said, you can't -- you can't -- that's a big jump. They don't show you -- I mean, they're just saying she had perineal exposure. Okay. And she has talc in these lymph nodes.
It doesn't mean that it went through the vagina, the cervix, the uterus, the ovaries, and somehow got into the lymph nodes.
BY MR. DEARING:
Q Well, these eight authors concluded that that exposure, the perineal exposure, is what resulted in the presence of talc in the lymph nodes; right?
MS. AHERN: Objection. Form.
THE WITNESS: They concluded that, but I don't see why -- they didn't give the alternate explanation, that it possibly got through inhalation. It makes more sense to me than coming through the vagina or the vulva -- from the vulva.
BY MR. DEARING:
Q Inhalation of talc particles depositing on

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ovarian tissue or pelvic lymph nodes is more plausible to you than perineal application?
A Yes.
Q Are you saying that inhalation of talc particles depositing on ovarian -- on ovaries or in pelvic lymph nodes is a biologically plausible mechanism of exposure?
MS. AHERN: Objection. Form.
THE WITNESS: Repeat that, please.
MR. DEARING: Sure.
BY MR. DEARING:
Q I believe you just said it was more likely, in your opinion, that the talc particles observed in the pelvic lymph nodes in this study got there through inhalation and -- as opposed to perineal exposure and migration.
My question is, by saying that, are you saying that it's biologically plausible that you can -- that a person can inhale talc and have those particles deposited on ovarian tissue or pelvic lymph nodes?
MS. AHERN: Objection. Form.
THE WITNESS: I didn't say anything about biologically plausible; I'm saying that I think it's more likely -- it's hypothesis. And that needs to be proven before it's accepted as being biologically

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plausible.
BY MR. DEARING:
Q So something can be more likely, in your mind --
A Yeah.
Q -- without being biologically plausible?
A Right.
Q And, of course, one of the advantages of using SEM-EDX, according to these eight scientists, is that it allows you to observe the talc particle in situ -- in other words, in the tissue -- not on the surface of the tissue; right?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I'm not an electron microscopist, so I can't really comment on their technology of avoiding contamination, which they, frankly, acknowledge could be a significant problem.
So I'd have to depend on someone who is an electron microscopist to really go over their methodology and say, oh, yes, this really is purified. I mean, cutting the section off the surface, I don't think that necessarily excludes contamination.
But, again, I'm not an electron microscopist. I think that needs to be evaluated by someone who is.
///

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BY MR. DEARING:
Q Right. Well, at least three of these authors are electron microscopists. So would you defer to them when they say that SEM-EDX methodologies is the best way to evaluate talc particles in situ or in tissue?
A No.
MS. AHERN: Objection. Form.
THE WITNESS: I would not defer to them. I would think you need an independent -- I mean, it's the same idea. It would have to be -- now, I realize the study got published, but I still would like to have someone else who's an electron microscopist to tell me to review that paper and say, yes, that makes sense. I can't do that.
BY MR. DEARING:
Q If there are three of the eight authors of this study who are electron microscopists saying that, why do you need more?
MS. AHERN: Objection.
THE WITNESS: It does -- I mean, they're -- I'm not saying necessarily biased, but they want to prove a case. So they're going to say, oh, yeah, this shows it.
I'd like an independent review by someone who is an electron microscopist who says yes, that's a

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reasonable way of doing it and avoids contamination. As I said, I'm not in a position to do that.
BY MR. DEARING:
Q Do you agree that the women studied in this publication who are in this study all claimed that they used talc for feminine hygiene?
A No, I don't think they all did. I think there were some that said they were exposed, but I think others said they weren't.
Q On page 3 at the top, the beginning of the first paragraph, it says "Talc is readily visible under polarizing light microscopy."
A Yes.
Q You agree with that; right?
A Well, that's what they say, yeah.
Q Well, you've --
A Oh, yeah, generally speaking, yes. Yes.
Q I mean, you understand how polarizing light microscopes work and how they will illuminate particles with birefringent properties?
A I use it.
Q And it also says that talc may be found as both plates and fibrous forms. And I believe you don't have an opinion about the fibrous forms; right?
A Right.

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Q And where the particles of fibers are brightly birefringent and often in the size range of 1 to 10 microns. We've already discussed that?
A Right.
Q And then do you see at the bottom of page 3, right-hand side, next-to-the-last sentence, it states what the eight authors' position was with regard to exposure.
It says "The birefringent particles present within lymph nodes were taken to indicate clinically significant talc that migrated there through the lymphatic system"; right?
A That's what they say.
MS. AHERN: Objection to form.
THE WITNESS: Yes.
BY MR. DEARING:
Q So we talked about migration through the genital tract. Do you have an opinion about whether perineal talc use can result in talc migration through the lymphatics to lymph nodes?
A Well, in order to get to the lymphatics, they have to get into the peritoneal cavity. So, as I said before, I don't believe -- and this, to me -- and this study doesn't prove it either, that talc particles on the perineum can get through the labia majora -- which

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are closed under normal conditions -- get through the vagina, get through the cervix -- which, most of the time, is closed to passage of bacteria, sperm, except at the time of the -- when women ovulate -- get through the uterus, get through the fallopian tubes, and get into the peritoneal cavity. I don't think that's possible. Unlike the lungs and the mouth, there's an open airway. That, to me, is more likely than going through that complicated route through the genital tract.
Q Do you also recall reading in this study that these eight authors suggested, and might have proved, that one of the flaws in the Heller study was that the technique used for determining the fiber burden in the ovarian tissue of the women was transmission, EM, in which they digested the tissue and thereby brought in the surface contaminants that Dr. Godleski and McDonald and Cramer and Welch and everyone else says that you have to be careful to avoid?
MS. AHERN: Is there a question? I'm sorry.
MR. DEARING: Yeah.
THE WITNESS: Yeah.
MS. AHERN: Objection. Sorry.
THE WITNESS: No, no. I think I'm getting -- please repeat the question.

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MR. DEARING: Sure.
BY MR. DEARING:
Q So one of the things this study addresses is the Heller study. And it's a continuation of the Heller study. And they're offering an explanation for why the burden count for talc particles in the Heller study seems to be inconsistent across the board with women who acknowledge being exposed to talc and women who either didn't know or -- or denied using talc.
A Correct.
Q Okay. And what they say in this study is that the problem with the Heller study was they digested the tissue and then counted the fibers. And by digesting the tissue -- or particles, talc particles, by digesting the tissue, you necessarily bring in surface contaminants so that the particles that you're calculating or quantifying are just as likely to be surface contaminants as anything else; right?
MS. AHERN: Objection. Form.
THE WITNESS: That's what they claim.
BY MR. DEARING:
Q Do you have any disagreement with them, with that analysis of the Heller methodology?
A I think --
MS. AHERN: Objection to form.

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THE WITNESS: I think that that's -- could be contamination, yes. That's what I said earlier.
BY MR. DEARING:
Q On page 11, they start summarizing their findings on the right-hand column --
A Hold it. Hold it.
Q I'm sorry. Page 13.
A Okay.
Q Right-hand column, three-quarters of the way down, it says:
"In the long-studied and debated association between talc exposure and ovarian cancer, our study provides additional evidence that talc may enter pelvic tissues and ultimately be detected and measured in regional lymph nodes, and this relationship became especially strong when clinical-use data was considered and surface contamination was corrected for statistically. This adds perspective to the known migratory capabilities and overall biological role/impact of talc."
Do you agree with the statement that the findings of this study provide additional evidence that

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talc may enter the pelvic tissues and ultimately be detected and measured in lymph nodes?
MS. AHERN: Objection. Form.
THE WITNESS: As I said a few minutes ago, I do not have the technical expertise in electron microscopy to critically evaluate the techniques that they claim avoided the contamination issue. So I cannot, at this point, agree with that.
BY MR. DEARING:
Q Dr. Cramer, who participated in this study, is an OB/GYN; right?
A Yes.
Q So with regard to a practical application of this study for an OB/GYN, the authors write:
"Our findings also suggest that in patients with ovarian cancer, clinicians may want to make broader inquiries into the past and present use of talc by their patients. Similarly, pathologists may wish to pay greater attention to sampled regional lymph nodes."
First of all, do you agree that, in light of the studies, whether you agree with them or not, and in light of the -- in light of the universe of studies looking at talc and ovarian cancer, do you agree that

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clinicians should consider broader inquiries with their patients about talc usage when they're suffering from ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: I'm not here to make recommendations for how patients should be advised.
BY MR. DEARING:
Q Well, do you agree that, since there are suggestions that pelvic lymph nodes may -- may gather or store foreign particles that may have contributed to cancer, to ovarian cancers, do you agree with the statement here that pathologists may wish to consider greater -- may wish to pay greater attention to sampled regional lymph nodes?
MS. AHERN: Objection. Form.
THE WITNESS: There's no data in this study to say, even if they were correct in saying that talc is in lymph nodes, that it has any bearing on the development of ovarian cancer. Nothing whatsoever. I've never heard of development of ovarian cancer based on material that's in lymph nodes.
BY MR. DEARING:
Q If that's true --
A It's biologically not plausible to me.
Q If that's true, why do at least three of your

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textbooks identify talc as a risk factor for ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: Well, a risk factor has nothing to do with its presence in lymph nodes.
BY MR. DEARING:
Q Well, risk factors have to do with a woman's increased risk of getting ovarian cancer; right?
MS. AHERN: Objection. Form.
THE WITNESS: It doesn't tell you anything about the mechanism, though.
MR. DEARING: I'm going to move to strike your last answer as nonresponsive.
BY MR. DEARING:
Q My question was, well, risk factors have to do with a woman's increased risk of getting ovarian cancer; right? That's the question.
MS. AHERN: Objection. Form.
THE WITNESS: I said, yes, increased risk. A truly accepted risk factor means that there's a risk of developing ovarian cancer. We discussed that issue of risk factors earlier and that there are weaker risk factors and stronger risk factors, and I would still adhere to that statement.
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BY MR. DEARING:
Q Do you know whether your new Blaustein's edition is going to identify talc as a risk factor for ovarian cancer, talc use?
A It will be mentioned, but not in the kind of detail that you asked me earlier. Again, to represent the broad, general notion of what's out there.
Q In the next-to-the-last paragraph in the last sentence, it says, "Our findings yield important insights as to the ability of talc to migrate to nodes."
A Wait, wait, wait. I'm not seeing it.
Q I'm sorry. Page 14.
A Yeah. Okay. 14.
Q Last sentence, next-to-last --
A "Our findings yield important" -- okay.
Q "Our findings yield important insights as to the ability of talc to migrate to nodes and under what conditions its identification to nodes and tissues is clinically meaningful and when not."
So do you disagree that this paper offers important insights as to the ability of talc to migrate to nodes?

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MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said earlier, I still am not -- since I'm unable to truly evaluate their procedure to prevent migration and to really pin down if talc is in ovarian tissues, I can't comment on the validity and my impression of this analysis.
BY MR. DEARING:
Q So we spent a good bit of time talking about your criticisms of Dr. Kane. Let me just ask you, do you have any criticism of her opinions that are not contained in your report?
A I think it's all there.
Q And with regard to her methodology for evaluating the issues of talc and ovarian cancer, you testified you have a problem with her methodology in that she relied on studies that you think should not have been relied on. Is that a fair statement?
MS. AHERN: Objection. Form.
THE WITNESS: Yes. Specifically, I said she relied on studies utilizing ovarian epithelial cells, surface ovarian epithelial cells, to bolster her argument that the studies that she cited were indicative of causation of ovarian cancer when I said that the private -- that the -- that the precursor lesions really were in the fallopian tube and that should have been the tissue

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that should have been used as -- to buttress our arguments.
BY MR. DEARING:
Q Do you have any other criticisms of her methodology as far as how she reached the opinions she reached?
A Well, as I said, there's some specific issues that I've listed in the paper. We've addressed some of them, like analogy. There's others that I mentioned as well. But, again, since it fails right from the beginning not identifying the appropriate tissue to study in terms of a precursor, everything else after it goes by the wayside.
Q As far as you know, have you identified all of methodological disagreements with her in your report?
MS. AHERN: Objection. Form. Asked and answered.
THE WITNESS: Well, in my report and what I've stated here in the deposition.
BY MR. DEARING:
Q Speaking of relying on the wrong studies, back to the migration -- I forgot to ask you a question.
So you relied on the monkey study and the mouse study, and I think you can see it may have little or no relevance to the human transmigration. But if you're going to consider animal studies to either

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support or refute the idea of talc migrating from the perineum to the ovaries or from the vagina to the ovaries, you didn't mention the Phillips study.
Are you familiar with the Phillips study? It's a rabbit study.
MS. AHERN: Objection. Form. Mischaracterizing testimony.
THE WITNESS: I would have to see it.
BY MR. DEARING:
Q You don't remember it?
A No.
Q It was a study where they injected talc into the vagina of a rat and discovered that it did migrate -- I mean of a rabbit, and discovered that it did migrate to the tubes.
Does that not sound familiar to you at all?
MS. AHERN: Objection. Form.
THE WITNESS: If you had the paper, it may jog my memory and I can comment.
BY MR. DEARING:
Q I don't have it. I'm just asking if you --
A Okay. Off the top of my head, I don't remember that particular study. I did evaluate a number of them.
But, again, just as you said, they introduced

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the talc -- was it talc that they used?
Q Yes.
A They introduced it into the vagina. So that immediately short-circuits one of the major barriers, which is from the perineum to get to the vagina. I mean, it's closed. The vulva is closed. The labia touch each other. Without physically opening them, something can't get into it.
Q Well, if talc could get inside the vagina, does that change your opinion at all about whether it can migrate further?
MS. AHERN: Objection. Form.
THE WITNESS: First of all, I would just repeat -- or say if it got into the vagina, and I'd say it can't get into the vagina.
BY MR. DEARING:
Q I know.
A And then there was a study that I cited in which they did -- let me see if I can find it. They put particles, not talc, into the -- where is migration? -- into the -- into the vagina. Let's see. I should be able to find that. Migration.
Okay. Here. On page 22, in the second paragraph. You highlighted it:
"It should be noted that even when

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particles are placed into the vagina, passage to the ovaries is quite unusual. For example, in another study it was reported that when India ink was introduction into the uterus, it was detected in the fallopian tubes in 50 percent of women and, when introduced into the cervix, it was detected in the fallopian tubes of just 30 percent of women. When it was introduced into the vagina, it was detected in only 1 of 37, 0.02 percent, patients. In short, the vulva is not an open conduit to the vagina and, therefore, none of these highly artificial studies can be used to assert that talc applied to the external perineum migrates to the fallopian tubes and ovaries."
BY MR. DEARING:
Q So your opinion is talc cannot get into the vagina under any circumstance; right?
MS. AHERN: Object to the form.
THE WITNESS: I said that, yes.
BY MR. DEARING:
Q So if a woman uses talc daily for feminine

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hygiene where she just pours talc in her panties, which a lot of these plaintiffs have done, and then she has intercourse that day, wouldn't that force some of the talc particles presumably into the vagina?
MS. AHERN: Objection. Form.
THE WITNESS: If it's still there, present at the time of having intercourse, I don't know.
BY MR. DEARING:
Q Well --
A It depends how much is there. I mean, it's totally speculation. I can't comment on that.
Q Is it biologically plausible that talc can be forced into the vagina if used externally --
A No, I don't think that's --
Q -- during intercourse?
A -- biologically plausible.
Q You don't?
A No.
Q This study that you're referring to actually supports what I was suggesting early on that you disagreed with me on, and that was that, if talc was introduced into the uterus, you said you still didn't think it would migrate to the tubes or to the ovaries.
But this dye did exactly that, didn't it? It was introduced into the uterus, and in 50 percent of

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the women it migrated to the fallopian tubes; right?
MS. AHERN: Objection. Form.
THE WITNESS: Of course, these are part India ink, not talc. So it's not a great substitute.
BY MR. DEARING:
Q Well, there are some materials, if introduced into the uterus, that would migrate at least half the time, according to this study, into the fallopian tubes; right?
MS. AHERN: Objection. Form.
THE WITNESS: India ink.
BY MR. DEARING:
Q Same question with the cervix. So there are some materials that, if introduced in the cervix, could migrate to the fallopian tube perhaps a third of the time?
MS. AHERN: Objection. Form.
THE WITNESS: Let's get down to the real -- real reality. When you get to the vagina, which is what you're talking about, introducing it in the vagina all the time, it occurred in 0.02 percent. Furthermore, that in and of itself is artificial, as I said. We're talking about perineal application, not introduction into the vagina, into the cervix, or into the uterus.
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BY MR. DEARING:
Q On your supplemental reference list -- I know you didn't prepare this list, but there's a study on this list entitled Sjosten. It's spelled S-j-o-s-t-e-n. And it's entitled "Retrograde Migration of Glove Powder in the Human Female Genital Tract."
In that study -- that study actually finds or found that talc deposited in the vagina from glove powder -- it was a starch powder -- migrated up the female genital tract.
Do you recall that study? Do you know that study?
MS. AHERN: Objection. Form.
THE WITNESS: Well, it's listed, but I haven't read that study. But, again, glove powder means it was placed into the vagina on pelvic examination.
BY MR. DEARING:
Q Right.
A Not on the vulva. Oh, and by the way --
Q It doesn't stay there. It didn't stay there in this study. It migrated.
MS. AHERN: Objection. Form.
THE WITNESS: From the?
BY MR. DEARING:
Q From the vagina.

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A We talked about that already, the vagina studies described earlier.
But I should also -- because you asked about sexual intercourse. And I could also -- I remember that -- it was an epidemiologic study. I can't, off the top of my head, remember which one, but I know that they evaluated talc in diaphragms, and that was not associated with an increased risk of ovarian cancer either.
MR. DEARING: Can we take just a quick break? I think I'm almost finished.
VIDEO OPERATOR BROWN: Time is now 5:59. Going off the record.
(Recess taken.)
VIDEO OPERATOR BROWN: Time is now 6:10. Back on the record.
BY MR. DEARING:
Q Doctor, in reviewing your report, I notice that your methodology for weighing the evidence on these issues that we've been discussing is not described.
Can you describe for me what your methodology is with regarding to weighing the evidence as it pertains to the causation, migration, inflammation, the issues we've been discussing?

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MS. AHERN: Objection. Form.
THE WITNESS: I thought I went over that methodology right in the beginning.
BY MR. DEARING:
Q Well, you talked about a general methodology based on your experience, your research; but you haven't explained how you actually weigh the evidence of the things that you consider.
MS. AHERN: Objection. Form.
THE WITNESS: Well, I read over Dr. Kane's report. I ran down her references. And, as I said earlier, the papers that she relied on did not assess or did not buttress her arguments about the causation of ovarian cancer based on talc usage because they didn't examine the right tissues. And I've said that before, and I still say that.
Then all the rest of it, like a set of dominoes, falls because, in order to establish causation, you need to look not at cancers, which many of the studies that she cited looked at because of increased inflammation, it's irrelevant. What you have to look at is the cell of origin of ovarian cancer, which we now acknowledge comes from tubal epithelium, and the studies that she looked at didn't analyze tubal epithelium.

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BY MR. DEARING:
Q Do you agree that, when a physician or scientist is assessing or forming opinions on issues like causation, inflammation, migration, that it's important for that physician or scientist to consider all of the relevant literature on those topics?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I don't know if you can ever say all of it. You try your best to read as much as you possibly can of the relevant literature and come to a conclusion.
BY MR. DEARING:
Q You agree with me that you've not done a comprehensive review of the literature on talc and inflammation?
A I'm sorry. Could you repeat that?
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q I said do you agree with me that you have not done a comprehensive review of all of the relevant literature on the issue of talc and inflammation?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said, I've reviewed many, many studies, and you can form an evaluation as these studies play out one way or the other. But all, every

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conceivable study? No, I didn't do that.
BY MR. DEARING:
Q Well, the studies that you considered are listed in your reference materials; right? Your two reference lists; right?
A Yes.
MS. AHERN: Objection. Form.
BY MR. DEARING:
Q In fact, some of the studies on the second reference list you didn't consider because you didn't even read; right?
A Right.
Q So if the studies aren't on your reference list, you did not consider them in forming your opinions that we've been discussing today; right?
MS. AHERN: Objection. Form.
THE WITNESS: That is correct.
BY MR. DEARING:
Q So is it fair to say that you did not do a comprehensive review of the literature regarding talc and its ability to migrate to the ovaries from the perineum?
MS. AHERN: Objection. Form.
THE WITNESS: No, I disagree. I think I did. In fact, I reviewed her studies which she claims supported

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migration, and I added other studies.
BY MR. DEARING:
Q With regard to the issue of inflammation, you had not seen the Saed study that we started to go over. You didn't recite the Ness 1999 study. You just saw the Godleski 2019 study for the first time today.
So there are significant studies that you did not consider in forming your opinions today; correct?
MS. AHERN: Objection. Form.
THE WITNESS: Well, I can tell you -- and I didn't analyze the Saed study because a number of other experts looked at it, and I did read their reports prior to this deposition and they felt that the studies were terrible, basically. And so I didn't find it necessary to review it. I found other experts reviewing it.
And right off the bat, he was looking at ovarian cancer cells, and that's not what you're supposed to be looking at when you're trying to establish causation of ovarian cancer. You don't look at ovarian cancer; you look at precursor lesions.
BY MR. DEARING:
Q Well, you've testified that epidemiology is not one of your primary topics that you plan to testify about.

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Would you agree with me that you haven't done a comprehensive search of the epidemiologic studies out there on talc and ovarian cancer; in fact, you only named a few in your reference materials?
MS. AHERN: Objection. Form.
THE WITNESS: Well, as I said at the beginning, in previous depositions and in the trial, I had reviewed many of the epidemiologic studies to, frankly, get up to speed on them because I -- up until 2015, I hadn't read all those studies, but at that time, I reviewed all -- you know, there was many that I thought were relevant. So I did review them at that time.
I didn't review them this time because I felt, well, I've done that in the past. And my focus at this deposition would be more on ovarian carcinogenesis from the standpoint of the gynecologic pathology.
BY MR. DEARING:
Q Are you aware that quite a few epidemiology study and meta-analyses have actually been published since 2015, since you testified?
A There have been some. And, like, I looked at some of these abstracts. Didn't look like it changed much.
Q Well, you haven't looked at the Taher study; right?

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A Can I see that?
MS. AHERN: Object to the form.
(The document referenced below was marked Deposition Exhibit 14 for identification and is appended hereto.)
BY MR. DEARING:
Q So this is the Taher study, and it's not on your reference list.
Have you seen that study before today?
MS. AHERN: You asked about published studies? Is that your question?
MR. DEARING: Studies.
MS. AHERN: The question was have there been other published studies that you did not review?
THE WITNESS: I have not seen this study.
BY MR. DEARING:
Q Have you reviewed the Health Canada assessment that was published on the issue of talc and ovarian cancer?
MS. AHERN: Objection. Form.
THE WITNESS: The only time I ever was aware of a Health Canada study was in reading the deposition of Dr. Kane. And she basically said, "Well, the findings in the Health Canada study agree with my findings."
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BY MR. DEARING:
Q You haven't read the Health Canada findings, have you?
A No, I haven't.
Q With regard to Dr. Saed's 2019 study, are you aware that one of the things he looked at and studied were fallopian tube cells?
MS. AHERN: Objection. Form.
THE WITNESS: I said I didn't read his study.
BY MR. DEARING:
Q So, no, you're not aware of the types of cells that he studied?
A No.
Q I think that's it.
A Okay. Thank you.
MS. AHERN: Okay. I have just have a couple -- or maybe one or two questions just for clarification.
THE WITNESS: All right.
MS. AHERN: Where is my note? Could you do me a favor and could you pull up time 15:14:19.
Hold on a minute. There you go.

EXAMINATION
BY MS. AHERN:
Q So, Doctor, you were asked repeatedly today

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about your opinions on ovarian cancer and talc and whether or not you thought talc caused ovarian cancer.
Do you remember throughout the day?
A Yes.
Q Okay. There are just a couple of question and answers that I want to go over with you, and then I'm going to ask you a question. And I think -- because we need some clarification on something.
You were asked the question:
"Would you agree that good scientists can have differing opinions about cancer etiology?"
And you responded:
"That's a very, very general question. But if I frame it with the talc litigation, I would venture to say that a reasonable scientist viewing -- viewing all, viewing the totality of this data, I don't think anyone would agree to say that talc causes ovarian cancer."
Do you see that?
A Yes.
Q Is that consistent with your opinions on talc and ovarian cancer?

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A Yes.
Q The next question you were asked by Mr. Dearing is:
"Are you saying that all of the plaintiffs' experts, the 30 or so plaintiff experts that you know about, are not good scientists."
And you said, "I didn't say that."
And then he asked you:
"Okay. Well, my question is do you agree with me that good scientists can have differing opinions about cancer etiology?"
You said:
"It's neither good or bad; I'm saying that reasonable people, looking at all this data, in my opinion, would not disagree that this is -- that talc causes ovarian cancer."
Is that consistent with your opinions on -- that you've given today on talc and ovarian cancer as it's written --
A That's a little bit of a confusing statement, I agree. It's kind of a double negative, "not disagree." So my view is -- I'm sorry.

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Q Sorry. And my next question was, in response to that question, what did you intend to say?
A What I had said earlier. And you can go back and cite the same thing again, that looking at the totality of evidence and data that's presently available, I don't think anyone would agree to say that talc causes ovarian cancer.
MS. AHERN: Okay. That's all the questions I have. Thank you.

FURTHER EXAMINATION
BY MR. DEARING:
Q Doctor, you just testified that you have not looked at the totality of all the evidence, that there are some studies you have not seen and have not looked at.
So do you agree with me that you have not considered the totality of all the evidence?
A Well, "totality," insofar as what is -- looking at available, but -- I didn't look at every single study, but I think if you put it all into perspective, as I mentioned when you asked me that earlier, is that you read a number of studies and things start to fall in place. And another one study isn't going to change it.

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MR. DEARING: Okay.
MR. ZELLERS: Thank you, everyone.
VIDEO OPERATOR BROWN: The time is now 6:23. This concludes the deposition. Going off the record.
(The deposition proceeding was concluded at 6:23 P.M.)

--ooOoo--

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CERTIFICATE
OF
CERTIFIED SHORTHAND REPORTER

The undersigned Certified Shorthand Reporter of the State of California does hereby certify:
That the foregoing proceeding was taken before me at the time and place therein set forth, at which time the witness was duly sworn by me;
That the testimony of the witness and all objections made at the time of the examination were recorded stenographically by me and were thereafter transcribed, said transcript being a true and correct copy of my shorthand notes thereof;
That the dismantling of the original transcript will void the reporter's certificate.

In witness thereof, I have subscribed my name this date:_____.

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PAMELA COTTEN, CSR, RDR
Certificate No. 4497
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After doing so, please sign the errata sheet and date it.
You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.
It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

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ACKNOWLEDGMENT OF DEPONENT

I,_____, do hereby certify that I have read the foregoing pages, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

_____

ROBERT KURMAN, M.D. DATE

Subscribed and sworn to before me this

_____day of_____,20___.

My commission expires:_____

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Notary Public

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